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## Monthly Message

One of the important groups in this office the Dental Advisory Committee does its work quietly and efficiently. The Committee came into being at the suggestion of Dr. Daniel Lynch, a Past President of the American Dental Association. Each year the Association is asked to submit to this office a panel from which to select members of the Committee which consists of the dental member of the Medical Advisory Council to this office, Dr. Thomas P. Fox as chairman, three members appointed by this office from the American Dental Association nominations (usually the President Elect of the Association is one of these) and the three Dental Chiefs of the military departments.

Since November 1955 this Committee has held eight meetings and has considered subjects pertaining to the dental profession, personnel, material planning for dental clinics and the operation of Public Law 569, the Medicare Act —reporting to the Advisory Council to the Assistant Secretary of Defense on the one hand and on the other to the Dental Advisory Committee to Major General Paul I. Robinson, MC USA, the Executive Director for the operation of the law. The Committee also cooperates with the American Dental Association and the Association of American Dental Colleges in the compilation of the Senior Dental Questionnaire and advises on the problem of foreign and American manufacture of dental equipment. Members of the Committee have taken many trips out into the field so that their recommendations are based upon firsthand observation and knowledge.

Dentistry is a part of the medical sciences and was in bygone years an integral part of medicine itself. The practice of dentistry is quite different, however, and has its own problems. It is with special pleasure therefore that I bring the work of this Committee to the attention of the dental and medical professions that they may appreciate the work the Committee performs and the questions with which it deals.

*Frank B. Berry*

FRANK B. BERRY  
Assistant Secretary of Defense  
(Health and Medical)

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## Foreword

The United States Army Medical Department and the Medical Department of the United States Army are proud to have the honor of publishing this book. It is the result of the efforts of the Medical Department of the United States Army, and the Medical Department of the United States Army, and the Medical Department of the United States Army.

FRANK B. BERRY, M.D.

Assistant Secretary of Defense (Health and Medical)

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# UNITED STATES ARMED FORCES MEDICAL JOURNAL

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## AN EPIDEMIC OF PLEURISY WITH EFFUSION IN BITLIS, TURKEY

Study of 559 Cases

FAHRETTIN ALPTEKIN *Captain Turkish Army Medical Corps*

**I**N 1955 an outbreak of an acute illness, characterized by basal pleurisy with effusion and typically following a benign course, occurred among the soldiers at Bitlis Garrison in Turkey. All cases differed from other types of pleurisy, especially in the common occurrence of basal pleurisy with effusion and in special features of the pleural fluid. My preliminary report<sup>1</sup> concerned cases observed in the first three months. This article presents a clinical description of the 559 cases seen over a period of 11 months, with a discussion of the differential diagnosis. Eight additional cases of pleurisy of the classical type were excluded from this study.

### OCCURRENCE OF CASES

After February 1955, patients with pleurisy with effusion were increasing in number every day, all men between 20 and 25 years of age. On some days there were as many as 20 new admissions to this hospital. There was no epidemic of any other disease among the soldiers either during or immediately before the outbreak of pleurisy.

The disease was first observed in the infantry regiment. Later it appeared in other units that did not have the same water supply and did not use the same kitchen. It occurred among soldiers

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From Bitlis Military Hospital, Bitlis, Turkey. Dr. Alptekin, now at Bird's College Hospital, Wilkes-Barre, Pennsylvania.

who had served in the army for from 3 to 21 months as well as among those who had been in service for only 20 days. The number of cases was greater in companies housed in close quarters.

The rapid increase in the number of cases and the fact that clinical and laboratory findings were similar in all cases made it evident that this disease represented an epidemic. The Corps Surgeon and later the Surgeon General were notified of the outbreak and two teams of bacteriologists were sent to Bitlis to investigate. They agreed that it was an outbreak of a contagious disease, the final report of the second commission being as follows. Although there is a probability of a non virulent primary atypical pneumonia which involves the pleura, it is recommended that sera be sent to the U S A for further laboratory studies.

The patients were isolated and the crowded conditions in the barracks were eliminated. This procedure appeared to have a significant effect in decreasing the number of new cases. The peak months were March, April, May, and June. The incidence was minimal throughout the summer, but increased somewhat in the fall and early winter (fig. 1). No new cases were seen after December 1955. As a result of the epidemic, the morbidity of pleurisy at Bitlis Garrison for 1955 was increased to 284 per thousand (table 1).

### PROCEDURES

The patients were admitted to this hospital from units in which the criteria for hospitalization were, in general, having an axillary temperature over 99.5 F or being at least moderately symptomatic. All patients were kept under close clinical observation and pleural fluid was withdrawn by thoracentesis. Smears made from every specimen were stained and studied carefully. Some of them also were examined by J. G. Scadding, M. D., Institute of Diseases of the Chest, London, England, and Ph. Schwartz, M. D., Warren State Hospital, Warren, Pa.

In 300 cases the following laboratory studies were performed: leukocyte count and differential, erythrocyte sedimentation rate, and examination of sputum for acid fast bacilli. The Mantoux test was done on 120 patients and control studies were performed on 200 subjects who were transient from outlying military posts and were normal, healthy soldiers. Blood serum from 55 patients was sent to Refik Saydam's Hygiene Institute, Ankara, for serologic testing to rule out Q fever and influenza. Roentgenographic examinations were made on only 30 patients because of a shortage

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1955) T m 2 C o l I S k T g M D L t C l I F b S r t M D d C p  
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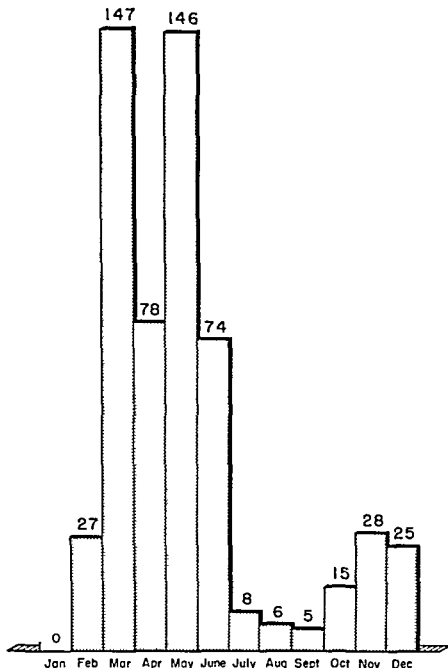


Figure 1 Monthly admissions of epidemic pleurisy cases to Bitlis Military Hospital in 1955

of x ray films, but fluoroscopy was carried out in an additional 150 cases

Inasmuch as it was not possible to determine the cause of this disease through the usual laboratory and serologic procedures, tests were made on guinea pigs and rabbits. Both nasal and peritoneal routes were chosen for inoculation of most of the animals. Histopathologic examination of the animals was performed at the Pathology Laboratory of Gulhane Military Medical Academy, Ankara, Turkey, the Pathology Institute of the Uni

TABLE 1 Pl y ca nd m b d ty at at  
B il H p tal 1953 1954 and 1955 Th  
g m t gth u a c tant t ab ut 2 000  
m th gb t th p d

Y	Numb of	Typ f pl urt y	M b d ty p r th d
1953	40	Cl i	20
1954	44	Cl	22
1955	8	Cl	
	559	Ep d m c	284

versity of Istanbul Istanbul Turkey and the Institute of Dis  
eases of the Chest University of London London England

### CLINICAL FEATURES

The clinical and laboratory findings were similar in all cases. The onset of the disease was usually abrupt and most of the patients were able to state exactly when they had become ill. Initial symptoms were cough malaise chilliness and fever anorexia headache and shortness of breath. There was sweating from time to time. The disease began with fever. The temperature ranged from 99.5 to 102° F during the first four to five days then returned to normal.

Patients complained of a nonproductive cough. Pain in the lumbar and thoracic regions of the back followed within a few days after onset of the initial symptoms. Usually at the end of the first week of the disease it was possible to determine by thoracentesis that there was some pleural effusion. Malaise was marked and patients complained of extreme fatigue weakness and exhaustion that caused them to be practically incapacitated.

At the onset of the disease slight facial and scleral injection were noticed and in typical cases tachypnea was obvious. It was quite possible to pick out these patients from a group of soldiers sent for examination just by looking at them.

Although there was a nonproductive cough and hoarseness sputum was scanty. However 40 per cent of the patients reported blood tinged sputum on two or three occasions during the first 10 days of their disease.

### Phys cal Fi di gs

There was pharyngeal injection. Dullness usually appeared at the base of the lungs approximately a week after the onset of the disease. This dullness usually could be elicited as high as a little above the angle of the scapula. There were many moist and dry rales especially in the basal regions of the lungs.

however, no pleural friction rub was heard. None of the patients had pharyngitis, conjunctivitis, lesions of herpangina, or adenopathy. There was no relationship between the back pain and deep inspiration. Some serofibrinous, light gray green fluid was aspirated by thoracentesis from the area of dullness in all 559 patients. We preferred the ninth intercostal space for the thoracentesis, because the chance of being able to obtain fluid was less at a higher space. Fluid was obtained from both sides in 111 cases, from the right side only in 212, and from the left side only in 236. The maximum amount of fluid aspirated from any patient was 15 ml.

The percentage frequency of occurrence of various symptoms and signs is shown in table 2.

TABLE 2 *Symptoms and signs in 559 cases of epidemic pleurisy*

Symptom or sign	Per cent
Cough	99
Malaise	90
Fever (within first 5 days)	75
Chilliness	75
Facial and scleral injection	60
Hoarseness	35
Abdominal pain	40
Anorexia	50
Headache	35
Blood tinged sputum	40
Low or high back pain	98
Rales in basal area of lungs	95
Pleural effusion	100

### Roentgenologic Findings

An enlarged hilar shadow was visible in 30 per cent of the patients. Although some pleural fluid was withdrawn from all patients, a small fluid shadow was observed at the costophrenic angle in only 5 per cent. It is known that as much as 300 to 400 ml of pleural effusion may not produce a shadow in a roentgenogram. In all patients the lung fields were normal (table 3).

### LABORATORY FINDINGS

The results of laboratory studies made on the patients are summarized in table 4.

#### Pleural Fluid

The properties of the specimens of pleural fluid that were obtained are shown in table 5. After leaving these specimens



TABLE 3 R l t f a d l g c x a m t f  
b t 180 p t t

R d l g f d i n g	N m b f	P t t
E l g d h l h d w	54	30
S m l l f l u i d h d w		
p h r t g l	9	5
C l l u n g f e l d	180	100

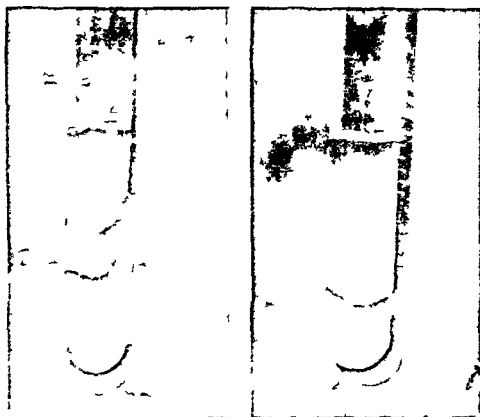
TABLE 4 S m m r y f r l t f l b t r y t d p t t u t h  
p d m c p l r y

P c d u r	R l	N m b f	P t t
E y h y t d m t r (W g r )	20-80 mm/h 13 20 mm/h	210 90	70 30
L u k c y t u n t	N m l B l w m l	195 105	65 35
D f l	L y m p h m y N m l	180 120	60 40
A d f t b l l i p u m	N g t	300	100
M t t e t O l O p t t	N g t P t	58 62	48 52
O 200 l	N g t P t	92 108	46 54
C o m p l m t f f Q f	N g a t P t e 1/16 P t 1/32	14 1 1	
H m g g l i n h b f f l I f l A I f l A (L) I f l B	N g t N g t i e N g t i P t 1/160 P 1/320	39 39 36 1 2	

in tubes for 1<sup>2</sup> to 24 hours a fibrous substance developed (fig 2) From 50 to 1 096 nucleated cells per  $\mu$ l of fluid were counted 60 to 70 per cent of these cells were monocytes according to Drs Schwartz and Scadding The remainder of the cells were lymphocytes and endothelial cells A few erythrocytes were noted

TABLE 5 *Typical properties of pleural fluid specimens withdrawn by thoracentesis from 559 patients*

Amount	10 to 15 ml
Color	Light gray-green
Rivalta reaction	Positive
Appearance	Serofibrinous did not coagulate After leaving in a tube fo 12-24 hours a fibrous substance looking like a spider web developed
Nucleated cells per $\mu$ l	50 to 1 096
Differential of these cells	Monocytes 60 to 70 per cent Lymphocytes and endothelial cells 30 per cent
Bacteria or acid-fast bacilli in smears	Negative

Figure 2. *Two samples of fluid withdrawn by thoracentesis from patients with epidemic pleurisy after standing for 24 hours. Note fibrous substance.*

A part of a report from Dr. Lynne Reid, Institute of Diseases of the Chest, Brompton, London, on the smears made from pleural fluid is as follows: "This pleural reaction being predominantly Lympho-Monocytic suggests either a lower grade chronic infection or an acute response to a virus infection. The clinical features of an acute illness make this last possibility the more probable."

## Animal Experiments

A summary of the animal experiments is shown in table 6. All of the animals died within 11 to 80 days after the inoculations and none had fever over 102 F.

Histopathologic reports of these animals did not indicate definitely that the disease was of virus origin; they did, however, establish that it was not tuberculous. The following histopathologic report from Dr. Reid concerns tests 7, 8, 9, and 10. The tissue from 4 guinea pigs has been sectioned. The liver and kidneys appear to be within normal limits. In the lungs there are occasional foci of haemorrhage and also diffuse peribroncholar cellular infiltration. This contains few polymorphs and consists mainly of leucocytes and macrophages. This material gives no real indication of the nature of the original disease, but it does at least seem to exclude the possibility of it being a tuberculous infection.

TABLE 6. Results of experiments on rabbits and guinea pigs

T Numb	T Animal	R fever		Infected		Remarks
		P only	N ally	Pl ur l f l (l)	P w h e n (l)	
1	Rabbit			2	2	Died 19 days after inoculation
2	Rabbit			2		Died 11 days after inoculation
3	Rabbit			2		Died 28 days after inoculation
4	Rabbit			2		Died 41 days after inoculation; facial scleritis
5	G Pig			2	1	Died 20 days after inoculation
6	G Pig			2		Died 63 days after inoculation
7	G Pig			2		Died 62 days after inoculation; facial scleritis
8	G Pig			2	1	Died 35 days after inoculation; pyrexia
9	G Pig			2		Died 69 days after inoculation; facial scleritis
10	G Pig			2	1	Died 80 days after inoculation; facial scleritis

## COURSE OF THE DISEASE

Illness lasted from 1 to 3 months. In 60 per cent of the cases the rales in the lungs disappeared in 10 to 15 days; in the remainder rales persisted for 3 or 4 weeks. The facial scleral

and pharyngeal injection and hoarseness disappeared within 10 to 15 days, however, cough persisted in most cases. The erythrocyte sedimentation rate returned to normal in 10 to 15 days.

The resorption of the pleural effusion ran a prolonged course in many cases. 3 to 5 thoracenteses were performed at intervals of 15 to 20 days for control of the fluid. Low and high back pain, chilliness, and weakness lasted for a long time. Weight loss was noticeable during the first month of illness.

Convalescence was considerably affected by cold weather, and there was exacerbation of symptoms upon resuming even light work. Some patients again showed the same symptoms and signs 4 to 8 months after their first illness, but we could not say definitely whether these represented reinfection or flare-up of the original disease.

Prolonged convalescence was a prominent feature of this epidemic. Most of the patients were unable to work for 3 to 4 months.

Prognosis was benign, and no deaths occurred. It was not possible to use a systematic medical treatment, but good results were obtained from symptomatic treatment.

#### REPORT OF A TYPICAL CASE

A 21 year old soldier from an infantry regiment was admitted to this hospital on 20 March 1955 with chief complaints of cough, chilliness, marked malaise, thoracic back pain, and anorexia. The patient had been well until two days prior to admission when he noticed the onset of chilliness, feverishness, malaise, and anorexia together with profound weakness and excess coughing.

On the morning of admission the patient noticed a small fleck of blood in his sputum. He had thoracic back pain but no sharp chest pain. His back pain was continuous and did not vary in intensity or severity. He had tachypnea, and facial and scleral injection that made it easy to pick him out from among the soldiers who were sent to the clinic. On admission his temperature was 100.5°F, pulse 92 and respiration rate 26 per minute. There was pharyngeal injection with out any exudate and hoarseness. Coryza was not present. Slight dullness was noted at the right base and there were abundant moist and dry rales at the base and lower part of the lungs. Adenopathy was absent and the remainder of the physical examination was normal.

On admission the patient's sedimentation rate was 56 mm at the end of the first hour. The white blood cell count was 7,600 per  $\mu$ l with a differential of 51 per cent segmented cells, 34 per cent lymphocytes, 14 per cent monocytes, and 1 per cent eosinophils. The reaction to the Mantoux test was positive. The sputum was negative for acid fast bacilli. A roentgenogram of the chest showed a prominent hilar shadow but clear lung fields.

Four days after admission 10 ml of light gray green colored sero-fibrinous Riv Ita positive pleural fluid was aspirated by thoracentesis from right base. In this pleural fluid specimen 876 nucleated cells per  $\mu$ l were counted of which 63 per cent were monocytes 25 per cent were large lymphocytes and 12 per cent were epithelial cells. Neither bacteria nor acid fast bacilli could be found in a smear.

After 24 days of hospitalization the patient was discharged to 3 months leave.

## DISCUSSION

Pleurisy is encountered frequently in military hospitals. Its cause especially in places where adequate laboratory facilities are not available is often assumed to be tuberculosis and management of the case is based on this assumption. Although tuberculosis is known to be the cause of pleurisy in perhaps 80 to 90 per cent of the cases there are numerous other diseases in which pleurisy may be seen. However I have not been able to find any mention in the literature of an epidemic of viral or infectious disease in which pleural effusion was a prominent sign in all cases as was true in the Bitlis series.

### Differential Diagnosis

*Tuberculous pleurisy* In all of our cases, the fever was of only short duration (4 to 5 days) at the onset of the illness but tuberculosis can produce various patterns of fever. The amount of pleural effusion was small in every case whereas in tuberculous pleurisy the fluid may rise to the upper border of the scapula. The quality of the fluid was in every case different from that typical of tuberculous pleurisy. It did not coagulate on standing in a tube for 24 hours contained mainly monocytes rather than lymphocytes or neutrophils and had very few erythrocytes. Pleural fluid injected into guinea pigs and rabbits produced no evidence of tuberculosis. There was no increase in the rate of positive reaction to tuberculin as compared with 200 normal controls.

*Epidemic pleurodynia* The clinical picture in all cases was quite unlike that of epidemic pleurodynia with its abrupt onset of severe paroxysmal pain in the region of the attachments of the diaphragm aggravated by movement and respiration. In epidemic pleurodynia there may be fibrinous pleurisy or the benign dry pleurisy described by Scadding but not pleural effusion. All reported outbreaks of epidemic pleurodynia have occurred in summer and early autumn whereas the height of the epidemic in Bitlis was during very cold weather in March with minimal incidence in the summer months.

*Q fever and primary atypical pneumonia* Both diseases are characterized by evidence of pulmonary infiltration, whereas the lungs were clear in all of the 180 patients examined radiologically. Serologic tests for Q fever were negative.

*Influenza* Hemagglutination inhibition tests for influenza were negative, and none of the patients had coryza.

*Undifferentiated acute respiratory disease and pharyngoconjunctival fever* In neither the undifferentiated disease described by the Commission on Acute Respiratory Diseases,<sup>6</sup> nor in the pharyngoconjunctival fever described by Bell and associates,<sup>7</sup> is there the characteristic pleural effusion seen in all of our cases. On the other hand none of the patients in the Bitlis epidemic had conjunctivitis, pharyngitis, or adenopathy.

### SUMMARY

An epidemic of an acute, febrile illness, characterized by basal pleurisy with effusion and following a benign course, was observed at the Bitlis Military Hospital, Turkey, in 1955. All of the 559 cases differed from other reported types of pleurisy and other kinds of acute respiratory disease, in the common occurrence of basal pleurisy with effusion and in various special features of the pleural fluid, including a predominance of monocytes among the cellular elements. Convalescence was prolonged; few patients were able to return to work sooner than 3 to 4 months after onset of their illness. Incidence was greatest in late winter, spring, and fall and was minimal in summer. Spread was most rapid in crowded quarters, apparently being mediated by air borne droplets. It seems most probable that this disease, tentatively designated "epidemic pleurisy," is caused by a virus.

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# SYSTEMIC VERSUS LOCAL FACTORS IN CORONARY ARTERY OCCLUSION

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WILLIAM F. ENOS J. M.D.  
JAMES C. BYER Cpt MC USA  
WILLIAM C. MANION M.D.

**H**OW can an atheromatous plaque exist for years and decades then undergo changes that may result in fatal disease sometimes causing death within a matter of minutes? The almost universal prevalence of atheroma is attested by recent investigations which have confirmed and extended previous studies showing that every person beyond the age of three years has atheroma of some degree in the aorta<sup>1</sup> and that by the end of the second decade over three fourths of all individuals have some atheroma in the coronary arteries.

In the succeeding decade or two, pearly plaques become the rule in both the aorta and coronary arteries. Yet decades may go by before complications ensue and in about half of the population no known disease referable to atherosclerosis manifests itself during the life span. What then precipitates disease? Is it a metabolic tide of systemic origin or a purely local circulatory disturbance such as vasoconstriction? We reasoned that if it were the former we should find similar changes around pearly plaques in other parts of the body whereas if it were the latter such changes would be absent.

## MATERIALS AND METHODS

A preliminary survey of histologic sections of aorta and coronary arteries in 7, unselected cases of recent myocardial infarction (age range 21 to 81 years) contributed to the Armed Forces Institute of Pathology disclosed sections of both the aorta and the coronary arteries in only 18 cases. In 7 of the 18, evidence of activity consistent with a metabolic tide could be found both in the aorta and in the coronary arteries. By "activity" is meant the presence of foam cells that appeared to be of recent vintage as indicated by their separate and distinct cellular outlines and their grouping in clusters and streaks beneath

the endothelium. We reasoned that these could be interpreted as the active phase of the lipogranulomatous process that goes by the name atherosclerosis, just as collections of plump epithelioid cells represent the active phase of the granulomatous process of tuberculosis. These preliminary results prompted further studies as follows.

The anatomic material from two additional groups of cases at the Armed Forces Institute of Pathology was reviewed (1) 106 of the 120 cases of coronary artery occlusion in the 18 to 29 year age group previously reported by Yater,<sup>3</sup> and (2) 49 cases of inanition obtained from the Dachau prison camp in Germany, which were selected for comparison because of the current interest in dietary factors in the pathogenesis of atheroma. The review of this material was supplemented by planned studies of two other groups of cases. (1) Sections selected from one or more atheromatous plaques in or near the aortic ring or in the ascending limb of the arch of the aorta were compared with sections from similar plaques in one or more of the coronary arteries in 30 asymptomatic cases in a comparable age group reported by Enos, Bever and Holmes.<sup>4</sup> (2) Multiple histologic sections from the fatal atheromatous plaque in a coronary artery were compared with multiple sections of atheromatous plaques in the aorta, in 5 selected cases of acute coronary artery occlusion.

None of the material could be considered ideal, but some of the missing links were minimized in the forward looking research as exemplified by the last two groups studied. For example, in the first 3 groups of cases (75 of myocardial infarction, 106 of coronary artery occlusion, and 49 of inanition) sections of the aorta were missing more often than not. Those that were present were presumed to be "routine" sections which were selected without a definite purpose in mind. Fat stains and formalin fixed tissues for frozen sections rarely were available. Hence, most of these surveys had to depend upon a study of routine sections stained with hematoxylin and eosin. In the planned studies (the last 2 groups), the histologic material included routine stains for fat (oil red O) and other special stains in selected cases.

### OBSERVATIONS

The results of the studies on the five groups of cases are summarized in table 1, and representative pathologic changes are illustrated in figures 1 through 4. "Positive data" consistent with the concept of a metabolic tide are recent foam cell collections in lesions of both aorta and coronary arteries, the latter presumed to have been taken at or near the site of maximum occlusion.

**Preliminary Cases of Recent Myocardial Infarction.** This group, as already mentioned, showed evidence consistent with a metabolic tide in 7 of 18 cases.





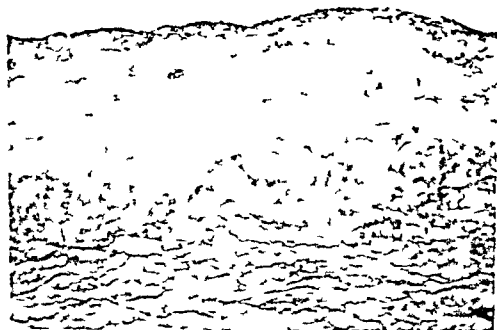


Figure 2. Aorta from same case as figure 1. Masses of lipid including conglomerate forms of foam cells beneath the endothelial lining (Hematoxylin and eosin stain  $\times 100$ )



Figure 3. Coronary artery from 30-year-old white man whose symptoms appeared less than one hour before death. Recent collections of foam cells in hyalinized intima of the coronary artery (Hematoxylin and eosin stain  $\times 200$ )



Figure 4. Aorta, same case as figure 3. Recent atheromatous deposit (conglomerate foam cells) beneath inner lining and medial layer reaction. (Hematoxylin and eosin stain  $\times 200$ )

only 41 of these cases. Recent collections of foam cells were seen in both aorta and coronary arteries in 19 (46 per cent) of the 41 cases. In 5 there was evidence of old thrombosis in 5 of recent thrombosis and in 9 of old and recent thrombosis. Extravasations of red blood cells and the presence or absence of phagocytosed hemoglobin could be correlated closely (16 of 19 cases) with the estimated age of the thrombosis. Old hyalinization of connective tissue about old lipid material is evidence for nearly plaque formation was present in all 19 cases. Occlusion of the lumen varied from 50 per cent to complete with 90 per cent or more of the lumen blocked in 16 of the 19 cases. All three of the major coronary arteries were involved with the most frequent site of partial or complete occlusion in the anterior descending branch of the left coronary artery.

In 9 additional cases the findings were equivocal for definite collection of foam cells in the aorta but with equivocal collections of foam cells in the coronary artery or vice versa or equivocal collection of foam cells in both locations. These 9 cases were not included in the 19 cases with "positive data." The clinical variations, especially manner of onset and duration of symptoms did not differ significantly in cases with and cases without positive data.

**Selected Cases of Acute Occlusion of Coronary Arteries.** An average of 52 sections of the coronary arteries and a section of

the aorta per case were studied in this small group of cases. As can be seen from table 1, the incidence of "positive" cases was high, but the number of cases is too small to warrant comment. The histories of the 3 "positive" cases in this group of 5 were carefully reviewed for any lead that might point to a metabolic tide. Two of the patients were men 30 and 31 years of age respectively, in whom the first attack was fatal, both were dead on arrival at the hospital. The onset of symptoms in both men was in the morning—one died in bed and the other in the bathroom—and the symptoms in each case lasted less than one hour. One was obese the other was not. Both gross anatomic protocols recorded small bright yellow nodules in the adrenal cortex. The third "positive case" was that of a white woman 26 years of age with hyperlipemia (1300 mg/100 ml) and hypercholesterolemia (575 mg/100 ml)—possibly familial—who had had a previous heart attack one year before the fatal episode. This case should be considered separately, leaving 2 of 4 cases "positive," with acute onset during rest or relative inactivity in young men the only possible indication of a metabolic tide.

**Dachau Internment Cases** Only 4 aortas were found among the histologic sections obtained from 49 prisoners of Polish, French, German, and Yugoslav extraction. Clinical histories were practically nonexistent. The principal cause of death was infection in almost all cases. No instances of coronary occlusion or myocardial infarction were noted. Body weight, which was recorded in 38 of the 49 cases, ranged from 70 to 135 pounds and was 100 pounds or less in 31. The striking feature of all the sections from the arterial tree was the total absence of foam cells. Practically all of the sections of heart showed extreme serous atrophy of subepicardial fat. The extremely thin intimal layer of the coronary arteries in these sections was in striking contrast with the thicker intimal layer in sections of the coronary artery from other groups. A few old hyaline plaques were noted in sections from both the aorta and coronary arteries, but again the total absence of foam cells was the feature of note.

**Asymptomatic or Control Cases** These came from 2 sources:

- 1 American soldiers killed in action in Korea. 20 cases of men 19 to 29 years of age, with 2 showing recent collections of foam cells in aortic and coronary artery plaques. These cases were from the group previously reported by Enos, Holmes and Beyer.<sup>2</sup>

- 2 Japanese cases obtained from the coroner's office in Tokyo and from the Department of Pathology at the Kyushu Imperial University Medical Faculty. 10 persons 14 to 45 years of age, 1 of whom had small recent collections of foam cells in plaques in both sites. Three females, 14, 16, and 20 years of age, all "negative," are included in the group of 10. The one "positive"

case was that of a Japanese man 35 years of age. These 10 cases were taken at random from the group recently reported by Enos, Bever and Holmes.

### DISCUSSION

Collections of foam cells have long been recognized as a distinguishing feature of atheroma. Hence the findings reported in this article of the presence of recent collections of foam cells in atheromatous plaques in both the aorta and the coronary arteries are not new in any sense of the word. Any merit that the findings may possess is dependent upon mechanisms and timing.

To discuss mechanisms first, it is obvious that the size of the atheromatous plaque can be increased and the size of the lumen correspondingly reduced by any of the following mechanisms: (1) increased filtration or inhibition of fluid or lipid; (2) increased local synthesis of lipid; (3) decreased outflow of fluid or lipid; and (4) any combination of the three.

These are the probable mechanisms of accretion, and this in itself is sometimes all that is found to account for a sudden or unexpected death. It also is possible that any of these mechanisms might put a relatively sudden strain on endothelial lined channels and their basement membranes to cause rupture, extravasation, and sometimes thrombosis. Thus accretion *per se* could account for ulceration, hemorrhage, and thrombosis. Furthermore the activity of certain chemical processes or even the mere presence of certain lipid substances might so alter surface tensions as to produce the vascular complications. Thus there are mechanisms of a systemic nature that could produce the same consequences as local vasoconstriction in or about the margins of an atheromatous plaque.

The finding of similar recent collections of foam cells in both aortic and coronary artery plaques with a frequency of about 45 per cent in those whose death was attributed to coronary artery occlusion, and with a frequency of 10 per cent or less in those whose death was attributed to other causes, lends some support to but does not substantiate the concept of a metabolic tide. That such collections of foam cells were not found in the other 55 per cent of cases with death attributed to coronary artery occlusion does not exclude their presence. Nor does it necessarily mean that local circulatory disturbances alone were responsible for the ulceration, hemorrhage, and thrombosis, for it is well known that certain individuals—even certain families and especially certain races—are more disposed to the early development of coronary artery occlusion. These individual, familial, and racial implications, however, are based on statistical analyses and do not come to grips with fundamental mechanisms. In general, they are more consistent with the concept

of metabolic tides than they are with the concept of local hemodynamic factors

Also in support of metabolic tides are two additional fragments of evidence obtained in this study (1) qualitative differences in the Japanese component of the control or asymptomatic cases, and (2) quantitative differences in the Dachau cases. In the Japanese cases, lipid was less conspicuous and less concentrated, stained a deeper red (had less of an orange tint) with oil red O reagent, and was more finely dispersed and more often extracellular than in the American cases. These differences have been noted previously<sup>4</sup> and probably reflect differences in dietary habits as well as racial peculiarities. The sections from the Dachau cases were noteworthy for their almost complete lack of foam cells. So striking was this feature as to raise a provocative question as to whether or not foam cells can be formed during inanition.

Possibly the best evidence for metabolic tides is the impression gained from review of the sections of aortas and coronary arteries from young adult males that lesions in the two locations are usually in the same phase or stage. If the aortic lesions were composed principally of altered ground substance, so, too, were the lesions of the coronary arteries. If the aortic lesions contained clusters of foam cells or basal grumous material, so, too, did the lesions of the coronary arteries. If two "crops" of lesions or evidences of accretion were found in one location, they usually were found in the other. Certainly, it was possible to encounter and describe differences, but it was easier to find similarities.

If obscurity shrouds some of the mechanisms involved in atherogenesis, it is even more difficult to describe and interpret the *timing of the sequence of events presumed to have been an integral part of the life history of the lesions we have reviewed*. For example, it is not known whether the process of atherogenesis in man is continuous or discontinuous, but the scant evidence available favors episodic accretion. This evidence is derived from the frequent finding—especially in the aorta—of "crops" of apparently recent lesions mingled with and superimposed upon obviously older lesions. This evidence has been substantiated in rabbits that have been fed cholesterol discontinuously over varying periods.<sup>5</sup>

The time required for the foam cells to appear and to form aggregations in man is not known, but in animals the process is usually described in terms of weeks. The earliest foam cells are said to appear within days, hence it is unlikely that the events of the preceding 24 hours would have an immediate influence on the collections of foam cells that we have emphasized in the human cases. The available data point to intermittent or

episodic metabolic tides with a periodicity punctuated by weeks rather than to ripples or waves punctuated by hours or days

Originally it was hoped that some confirmatory clinical evidence might be gathered during study of the human cases with recent foam cell collections in both aorta and coronary arteries but the recorded observations were incomplete on many significant points and the only positive suggestion was the rapid onset of symptoms and fatal outcome in young males while at rest or shortly after arising from bed. It is possible that a careful study of nonfatal cases might yield clues and that alerted clinical suspicion coupled with selected chemical determinations at critical times might yield useful data reflecting the metabolic tides suggested by the anatomic data presented in this paper

### SUMMARY

An attempt has been made to assess the role of systemic versus local factors in the production of coronary artery occlusion by studying sections of aortas and coronary arteries in three groups of cases and two groups of controls at the Armed Forces Institute of Pathology. Some evidence was obtained to support the concept of a metabolic tide in nearly one half of the cases with coronary occlusion.

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## EVALUATION OF AMNESIA IN BRIG MEDICAL PRACTICE

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“WE WERE in Japan. One night there was trouble and it became a fight. I vividly remember getting hit on the head. When I came to I was in Philadelphia and it was months later.” This was the explanation offered by a young Marine who was awaiting court martial for being several months absent without leave (AWOL).

Amnesia is a frequent complaint among servicemen confined in the brig for AWOL. It presents a diagnostic problem because among the many amnesic antisocial personalities and malingerers there is always the solitary and unusual case of dissociative reaction with amnesia and fugue (running away). Like a neurotic with a back pain, any inmate who complains that he lost his memory is entitled to a comprehensive medical and psychiatric examination.

Aside from the responsibilities of the medical officer that are inherent in his profession, there are legal aspects to be considered. It is a travesty of the public trust to drop the charges—most often AWOL—in the case of the antisocial personality claiming amnesia. This would suggest that he is the victim of a disease process which absolves him of legal responsibility and might necessitate his discharge from military duty—a situation that would result in financial loss in the form of the cost of his training and equipment and the cost of his subsequent pension.

On the other end of the scale, it would be unjust to imprison a man who has lost control of himself and his identity for a period of a few days because of overwhelming anxiety related to his presence in military service. In such a case the individual is unaware of the nature or consequences of the act, although later he is able to participate in his own defense.

Thanks to television and numerous novels such as Hilton's *Randori Harvest*, amnesia again has become a popular symptom. The relative decline of cases between the first and second world wars was ascribed to a growing public sophistication. Perhaps



this trend is being reversed through the efforts of modern unsophisticated entertainment such as TV and comic books. In any case, one finds amnesia a frequent complaint among antisocial personalities. True fugues are more unusual. Principally because of the problem of disposition, it is essential for the medical officer to make a differential diagnosis when the inmate first arrives at the brig.

The main point of differences between an antisocial personality and a case of fugue based on dissociative reaction—both men claiming amnesia—lies in the mechanism behind the major symptom. For the antisocial personality, the reliving of an amnesic episode is the result of an attitude of impulsive opportunism with the prospect of secondary gain (his release). The individual is consciously aware that he did not truly lose his identity. For the dissociative reaction (psychoneurotic), the episode was the consequence of overwhelming stress on the psychobiological organism.

Since one cannot reach a defensive mechanism of the ego directly, the diagnosis must be established by differential means. Naturally, a good longitudinal history would help to establish the diagnosis. The antisocial personality often has a pruricity of deep outside interests and a long history of rebelliousness, impulsiveness, difficulties in school and with the law. There is an over-all and consistent pattern to his social relations that is quite in contrast with the dissociative reaction type. A discussion of these differences is not pertinent to the problem of making an immediate differential diagnosis in a man who claims amnesia as the basis of having been AWOL. Unless at the time of examination a longitudinal social service history is available, a differential diagnosis must be made on clinical grounds alone. These two psychiatric entities will be compared using the format of the mental status evaluation.

### ATTITUDE AND GENERAL BEHAVIOR

Antisocial personalities are generally possessed of better than average dramatic abilities. Their appearance in the examining room can vary from wild-eyed excitement to profound depression. The medical officer must use all his art to disarm the patient of his defenses. An innocuous and nonpersonal discussion of the conditions in the brig, a cigarette offered to the inmate or mention of the furnishings of the office might be the first step.

Both antisocial personalities and dissociative reaction types are alert to the interviewer, but the antisocial personality has a peculiar piercing attentiveness in which he actively and consciously sizes up the interviewer, gauging his caliber and estimating his weaknesses. As the interview progresses, the antisocial personality will assume control and direction of the talk.

avoiding some things, stressing others. The interviewer feels that he is in the presence of a subtle super salesman. This is in contrast to the dissociative reaction type who is passive to the interview, permits himself to be directed in the discussion and is aware of the doctor but does not adapt himself quickly to what he thinks is the type of person interviewing him. This social faculty of adaptation and of manipulation of people seems to be notable in antisocial personalities and probably is the basis of their manifest charm.

As the antisocial personality is put at ease one notices a variety of facial expressions intended to be appropriate to the circumstances but not seeming to be genuine. It may seem to the doctor that the patient is trying to appear distraught and "intense." The anxious patient either appears dazed in expression or smiles a great deal because of obvious apprehensive restlessness.

In such an interview where one is trying to assay the underlying character structure of an inmate who claims amnesia it always is helpful to gently steer the conversation to sex. The antisocial personality if not suspicious of the doctor's motives is likely sooner or later to boast of his social successes with women. Such persons have little hesitancy about discussing sex and if the doctor simulates a modicum of naivete he will encourage the patient to reveal a fairly fundamental diagnostic point. Aside from boasting and lack of hesitancy the antisocial personality may well describe a pattern of sexual behavior that is impulsive, varied and poorly integrated. Homosexual episodes, seductions, relations with prostitutes, all are revealed without remorse, shame or any affect of noticeable intensity. In contrast patients of the dissociative reaction grouping are rarely boastful about their sexuality or even moderately successful in their efforts at seduction. Because of an exaggerated concern for appearances and a basic shyness the anxious psychoneurotic type will avoid a discussion of sexuality. Even when involved with the topic he is inclined to be evasive and embarrassed.

A similar diversion can be made to discuss policemen and the law. The antisocial personality if not suspiciously evasive can be drawn into a discussion in which he will reveal strong feelings of contempt, disdainful amusement, or deep hostility for the forces of law and order. He might take the initiative to enlighten the seemingly "square" doctor with a few personal experiences in which he came to grips with the minions of the law. As would be expected from the dynamic differences between these two character types the individual with dissociative reaction avoids all contact with the law because of his basic apprehensiveness and because he feels the need to conform to social structure. If anything he envies the police and secretly wishes that he could be as heroic in his behavior.

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be shy, very quiet, and seems inoffensive to the guards. He probably is noted to avoid the louder inmates and to be careful about staying out of trouble. Although he can become angry about what he feels is an act of injustice, he is inclined toward compliance to regulations—even in the prison. A careful documentation of the amnesic's behavior while awaiting trial can be an important foundation to a diagnosis which will, in all probability, be questioned at court-martial proceedings. In the eyes of the judges specific examples of behavior lend greater validity to a diagnosis than does medical opinion.

A further point of differential diagnosis on the behavioral level lies in the countertransference. This cannot be used in court testimony but is important in the practice of medical art. The medical officer often feels in talking to antisocial personalities, that he is being cleverly manipulated. The doctor generally does not feel a surge of empathy toward the patient, but rather an inner sense of emptiness as he gropes in interview, for the psychological essence of the patient. The patient's explanations in response to pointed questions seem plausible enough until the doctor stops to ask himself "Would I have done it that way?" He begins to believe that the patient's actions are based on impulse rather than on overwhelming anxiety or on reason. This lack of empathy and difficulty in understanding the thought and action of the antisocial personality is in contrast to what he generally feels toward the dissociative reaction type of person. Here he finds himself feeling somewhat sorry for the inmate's predicament and finds himself trying to reassure and relax his patient. The doctor interjects words, supplies phrases, and perhaps becomes a little patronizing. The physician might decide that he could experience the same reactions in response to the same stressful situations although he cannot imagine himself being so overwhelmed as to lose his identity and all awareness of his behavior. The countertransference is not a point of "scientific evaluation" but because it enters heavily into every diagnosis anyway, it might well be utilized as an additional point of clinical differential diagnosis.

### MECHANISMS OF THOUGHT

Inasmuch as both types of disorder are basically nonpsychotic a disturbance of thought is not easily elicited. Persistent questioning and conversation with the antisocial personality might reveal a repetition of circumstances such as difficulty with authority where the individual seems to fail to profit from his experiences. Eliminating compulsive behavior based on delusions or hallucinations (as one might see in schizophrenia) one discovers that the individual is compliant to impulses and fails to profit from the consequences of his behavior. In contrast to this the dissociative reaction type is rarely impulsive and tends to be markedly affected by his experience as revealed by the pattern of his life in the past.

The differences between these two clinical types are not easily elicited but as mentioned before the antisocial personality thinks and acts quickly adjusts himself to a provocative question with a spontaneous prevarication—something seen much less often in dissociative reaction types. The antisocial personality is almost always an unreflective type of individual who asks himself few questions. This defect can be elicited when he is asked for the reasons behind his behavior. His answers seem to be created on the spur of the moment and not to be the result of deliberation under more quiet circumstances. The dissociative reaction type is more thoughtful but rarely to the degree of the obsessive compulsive character. He can explain his behavior with the exception of the amnesic episode. One also senses in interview the marked indecisiveness of the dissociative reaction type. A further difference in types of thinking might be discovered by questioning the patient regarding reasons for past indiscretions. Antisocial personalities are more inclined to be righteous in the sense of believing that they acted correctly while the dissociative reaction individual feels it is he who is out of step with the world admitting to grave errors in judgment in the past.

#### EMOTIONAL RESPONSE

If a report of the inmate's behavior in the brig is available the demonstration of a bad temper is suggestive of an antisocial personality. The most significant difference in the area of affect between these two types lies in the basic lack of warmth of the antisocial personality. One believes that these patients imitate and express the manifestations of emotion but harbor a deep and unremitting emptiness beneath. If the medical officer is reluctant to utilize the countertransference as a point of clinical diagnosis a review of the patient's history as related by the inmate may reveal a paucity of deep interpersonal relationships—he just doesn't get involved with people. In contrast the dissociative reaction type struggles to conceal his lively affects using the defense of the blank facies and might admit that he is too emotional. He might cry if under stress or become quite depressed during his confinement.

Antisocial personalities generally show greater psychomotor activity in the brig and almost never are withdrawn except during interview when they are forming emotional illness. Any attempted suicide is likely to have more serious intent in the dissociative reaction type than in the antisocial personality who impulsively will wrap trainings around his neck swallow buttons or go on a hunger strike. A minor point might be explored in reference to animals and pets. Dissociative reaction types are more inclined toward compassion sympathy and attachment to animals often to the point of being very hostile to anyone who abuse them. Anti

social personalities do not have this degree of emotional warmth and are casual or indifferent about animals, their sufferings, et cetera

Antisocial personalities rarely show any seriousness of purpose in their behavior. They develop no skills, strive for no professions and never apply themselves. The more socially oriented dissociative reaction types are more "outwardly directed" and try to mold themselves to the social concept of skills, self support and responsibility. They are also more inclined to have some over all plan for their lives and toward which they are striving. This aspect of life is dealt with superficially and opportunisticly by the antisocial personality.

### CONTENT OF THOUGHT

Differences between these two types are not striking in this area. One finds the antisocial personality more prone to place the responsibility for his circumstances on others as mentioned above. He has little interest in moral or ethical problems and cares little for abstract discussion. He is also inclined to exaggerated notions as to his charm, abilities, et cetera particularly in reference to women.

The antisocial personality is more likely to feign "hearing voices" and "having visions"—often a complaint too easily believed by psychiatrists who fail to look for accompanying anxiety or the effect of hallucinations on behavior.

### SENSORIUM INSIGHT AND JUDGMENT

Whereas the dissociative reaction type might show poor judgment because he is intellectually dull the antisocial personality frequently demonstrates a defect in judgment based on his semantic aphasia and disorder of thought. He never quite grasps what important emotional experiences mean to others, and because of this does not have the capacity for empathy. He is more inclined to rationalize his behavior *post factum*, and seems to have a very shallow image of himself rarely going beyond the level of self aggrandizement. Seldom does he express any sincere concern for what he is. This is in contrast to the dissociative reaction type who is chronically more dissatisfied with himself. Antisocial personalities rarely show efforts for change or self improvement in their life pattern.

### SUMMARY

Amnesia is a common complaint among servicemen confined in the brig and charged with offenses such as absent without leave. Cases of amnesia with organic causes rarely are seen in the brig because they are hospitalized elsewhere. It is important to establish whether or not the complaint is a genuine one. This often is determined by the underlying character struc

ture. In individuals where anxiety is strong there may be a true dissociative reaction with fugue. Such overwhelming tension could be an extenuating factor in considering responsibility for the infraction of regulations. On the other hand the compulsion of amnesia in an anti social personality often is a fabrication and has nothing to do with the reasons for the offense in question. Medical opinion as to whether the individual was aware of the nature of the act when he committed it" must be based on the character structure of the man in question. Such a differentiation between a true amnesia with fugue and the simulated one seen in antisocial personalities can be on a clinical basis. Careful evaluation and documentation in the health record is important when the medical officer is called upon to give medical testimony in court martial proceedings. An error in diagnosis will result in miscarriage of justice in the case of the amnesic dissociative reaction with fugue or in financial remuneration of the conscientious violator of service regulations in the case of the antisocial personality.

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#### THE PHYSICIAN'S ASSISTANT

Every physician ought to remember that parents and especially mothers are the ones who repeatedly take care of the suffering of their children during their minor illness and injuries and that they continue this nursing function even through dolence. They turn to physicians for their professional service only when the nature of severity of an illness or injury is too serious for them to manage. If hospitalization is not necessary or not possible the physician must depend upon the child's mother to function as his nurse. His influence like the influence of immediate relatives in other situations is of great importance in the medical treatment of the sick child. Her confidence and trust in the physician increase his therapeutic intent and in transmitting her positive feelings about him to his patient she strengthens her child's faith in the physician. The same favorable influence on the physician may be observed when the significant relative of an adult patient admires and respects him. If however the mother of a sick child or the immediate relative of an adult patient mistrust, depreciate and dislike the physician they thereby diminish his personal influence with his patient and the effectiveness of his treatment.

—LEO H. BARTEMEIER, M.D.  
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# TREPONEMA PALLIDUM IMMOBILIZATION TEST IN THE FAR EAST

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THE *Treponema pallidum* immobilization (TPI) test was initiated as a diagnostic service at this laboratory in January 1955. This was the first use of the test on a routine basis anywhere in the Far East. The TPI test is a specific serologic test for syphilis and other treponemal diseases, based on the immobilization or killing of living, motile treponemata mediated by treponemal antibody in conjunction with complement, whereas the basis of the Wassermann test and its many modifications (serologic tests for syphilis, or STS) is not clear, and positive results in these tests may be unrelated to treponemal infections. This is not unexpected inasmuch as the STS are based on the reaction of substances in test serum, usually designated as Wassermann roagin, with phospholipid constituents of normal tissue.

From a technical point of view, the only serious difficulty encountered in establishing the test in Japan was the requirement for a mixture of nitrogen and carbon dioxide gas. Those obtained from Japanese sources were toxic to treponemata, making it necessary to import gas mixtures from the United States.

The test procedure at this laboratory was established by Dr Ruth A. Boak of the University of California at Los Angeles, and performed as outlined by Peterson, Asch, and Boal.<sup>1</sup> The reproducibility of the test procedure, as determined by the quantitative testing of a reference serum on different days, exceeded that reported in several publications. One such serum, tested 15 different times, gave a mean titer of 36.9 with a standard deviation of 13.8.

The value of and indications for the TPI test have been discussed in the literature.<sup>2,3</sup> Perhaps the greatest value of the

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their giving none in the cardiolipin complement fixation test. These 33 specimens reacted to some degree, however, in the cardiolipin microfloculation test, which is adjusted to a higher level of sensitivity than the cardiolipin complement fixation test.

It should be emphasized that the correlation of the results between the Wassermann tests and tests for treponemal immobilization antibody is a function of the sample tested. Specimens were submitted from all U S Armed Forces medical installations in the Far East Command, so that the sample was essentially random and undefined except for a TPI test requirement. In it, individuals of all types were represented: military personnel, U S Civil Service personnel, American and Japanese dependents of U S military personnel, a few Koreans, and hospital patients. Samples exclusively from hospital patients, from venereal disease treatment centers, or from specific geographic areas of the world might result in correlation of an entirely different type.

#### RESULTS IN ORIENTALS

Prior to the introduction of the TPI test, our data had shown that a significantly greater percentage of routine specimens from Orientals than from Americans reacted in the STS. These results indicated either a greater reservoir of syphilis or a greater incidence of biological false positives among the Orientals. The TPI test provided evidence that the former interpretation was the correct one. In the American sample, 56 per cent of 191 specimens, all from different individuals, that reacted in the cardiolipin microfloculation test also reacted in the TPI test. In the Oriental sample, 61 per cent of 232 specimens that reacted in the cardiolipin microfloculation test also reacted in the TPI test, and 77 per cent of 120 specimens that reacted in the complement fixation test also reacted in the TPI test. These differences between the Oriental and American samples were not significant at the 5 per cent level by the chi square test.

The Oriental sample consisted almost exclusively of specimens from Japanese dependents of military personnel and Japanese employees of the U S Armed Forces, and, as suggested by several Japanese investigators, the high reaction rate in both the standard STS and TPI test may not reflect the situation in the Japanese nation. Be that as it may, we are not aware of any reason why the percentage of biological false positive reactions in the STS should differ appreciably in our sample from what would be found in testing other persons in Japan. The STS reaction rate in any Japanese population, therefore, probably should provide a true index of the incidence of syphilitic infection.

Various studies have indicated a particularly high prevalence of biological false positive reactions among certain racial groups such as the North American Indian the Negro the laboring class in Mexico, and the Guatemalan Indians.<sup>4</sup> These observations probably are valid although the studies were performed without benefit of the TPI test. The results obtained at this laboratory however do not indicate that the Orientals tested had a particular predilection for biological false positives at least as compared to the Americans tested.

### SUMMARY

Although the *Treponema pallidum* immobilization (TPI) test is highly complex and requires well trained technicians for its performance it has been established successfully in the Far East, and there is a steadily increasing demand for its use. Valuable in the detection of biological false positive reactions it has in many instances indicated the existence of a present or past syphilitic infection in individuals whose reactivity in the standard tests might otherwise have been disregarded. The TPI test also has indicated the probable validity of the standard tests as an index of syphilitic infection in the Orient.

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# KLEPTOMANIA

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**K**LEPTOMANIA is a condition characterized by repeated episodes of stealing that are considered to be nonpredatory and are the result of strong unconscious forces compelling the individual to commit the offenses. Psychiatrists and other medical officers in the military service are frequently called upon to examine an individual caught stealing and to determine whether or not the offense represents a case of common theft or a case of theft involving unconscious motivation. The differentiation between the predatory thief and the kleptomaniac, although not always important in a medical sense is nevertheless an important issue because of its legal implications. The *Manual for Courts-Martial* states

A person is not mentally responsible in a criminal sense for an offense unless he was at the time so far free from mental defect, disease, or derangement as to be able concerning the particular act charged both to distinguish right from wrong and to adhere to the right.<sup>1</sup>

Whether or not the individual was moved to steal because of an irresistible impulse and therefore could not adhere to the right is usually the most important legal consideration facing the psychiatrist in evaluating persons accused of theft. Harpman<sup>2</sup> stated that kleptomania must be viewed as a symptom of a neurosis and therefore it is senseless to punish the individual displaying this symptom. In some cases he pointed out it is the expression of an overt psychosis. The underlying unconscious motives causing the condition called kleptomania can be brought to light by psychiatric examination. The following are case histories of patients exhibiting kleptomania.

## CASE REPORTS

**Case 1** A 21 year old unmarried U S Marine Corps corporal was caught stealing money from the trousers of other marines in his barracks. When apprehended he ran wildly through the barracks, leaped from a window, attempted to bury the money in the ground and then returned to his bed pulling the bedcover over his head. He was taken into custody and awarded a Special Court Martial. While in the brig he appeared emotion

ally disturbed and a psychiatric consultation was requested. When first examined he appeared in panic. He cried uncontrollably and demonstrated marked blocking and confusion associated with an inability to recall clearly recent events. Admission to the hospital was advised. Only after several weeks of hospitalization was a significant reduction in his anxiety achieved.

Past history revealed that the patient had stolen frequently since attending the eighth grade of school. He had been punished physically on several occasions when thefts were discovered by his parents but this only served to increase his need to steal. Usually the patient stole money but at no time did he break into a building plan his thefts beforehand or join other with the intent to steal. He always possessed sufficient spending money and usually disposed of the stolen money by throwing it away or buying gifts for his parents. The theft was always an impulsive act and usually very obvious. It was under situations of stress such as starting school or punishment by his parents that he was most likely to steal. His parents were unaffectionate and overly punitive. The patient's father was rigid and compulsive individual who insisted on strict obedience to his demands. The mother expressed affection only by giving him small sums of money. She frequently referred to him as a "thief" and "kid". She would often misplace her purse and then accuse the patient of stealing it stating "Once a thief always a thief." It is noteworthy that each of the patient's three older siblings had been involved in considerable antisocial behavior.

This patient suffered from marked feelings of isolation, rejection and held a deep seated hostility toward his parents. On mental status examination he appeared to be a schizoid personality type who had a great need for affection. This need along with dependency need was opposed by feelings of hostility, guilt and rejection rendering him unable to make lasting or mature relationship with people. Under sufficient stress he experienced anxiety of panic proportions associated with confusion, withdrawal and inaccessibility. At those times he would steal and the anxiety would be lessened. During the latter half of his hospitalization the patient was permitted to go on liberty and he only occasionally experienced an easily controllable desire to steal. After five months of psychotherapy he was honorably discharged from the U S Marine Corps.

C 2 An 18 year old married Navy airman was seen opening sealed mailbag and removing package. The event occurred at night aboard ship and appeared to have been done without any consideration as to who might be watching. He was followed and was found sitting in a room with the partly opened package in his lap. When apprehended he seemed to regain contact with the environment suddenly and claimed no recollection of how he came to possess the stolen package. A General Court Martial was ordered but in view of the unusual behavior associated with the theft psychiatric consultation was obtained. As a result of the consultation and subsequent study upon the patient's mental competency at the time of the act the patient was hospitalized.

Past history disclosed that this individual had been regularly stealing since the age of 13 at which time he discovered a baseball glove secreted in his sweater after he walked out of a sporting goods store. Many instances of theft followed but at no time could he actually recall the act of gaining possession of the stolen article. Several times he removed money from his father's pocket and was beaten by the father. After enlistment he continued to steal money and served 51 days in the brig when he confessed to one of his crimes. Following completion of the tenth grade in school he married and at the time of hospitalization had a child one year of age. He was reared in an inimical family setting where there were frequent open clashes between the parents. The patient's father was described as a miserly man who hoarded his money and deprived his wife and children of many basic needs. At times however he would foolishly spend money for his own entertainment. According to the patient his father was extremely critical of the infidelity of others but he himself frequently would be openly flirtatious with women. In addition to physically abusing the family he imposed many restrictions which led to minor conspiracies between the mother and son in their attempt to outwit him. For example the patient and his mother would secretly smoke cigarettes together and exchange gifts. The patient's wife was never accepted by his mother who expressed her resentment by avoiding her. She also continued giving her son gifts for his own personal use while ignoring his wife.

The patient suffered from severe anxiety attacks and on occasion experienced dissociative like episodes not accompanied by stealing. Generally he exercised suppression and withdrawal to handle his problems and hesitated to believe the reality of the situation. He was hospitalized for three months part of the time on an open ward and at no time did he commit a theft. It was believed that this patient was a latent schizophrenic and was not responsible for his actions at the time of the offense. The charges against him were dropped and he was awarded an honorable discharge from the Navy.

**Case 3** A 21 year old unmarried Navy seaman was transferred to the hospital after he confessed to the theft of numerous articles belonging to his shipmates. A search of his locker revealed many stolen small items such as cigarette lighters fountain pens and clothing. No disciplinary action was brought against him and upon recommendation by the psychiatrist he was hospitalized.

This patient began to steal when he was 10 years old and continued to do so frequently except for one period during his last year of high school. In every instance of theft the patient was unable to recall the act of stealing the acquired item but only later would find the article in his possession and then realized that it had been stolen. Frequently he would remain in the company of another person in the effort to avoid stealing but when alone he exercised no control over his actions. Often the patient returned or paid for the stolen merchandise but in the months prior to hospitalization especially while in the Navy he was unable to do that for fear of punishment. Fountain pens and "flashy" cigarette

lighters were the most frequently stolen articles. He was caught on only two occasions and was able to lie his way out. While in the Navy he was considered to be a chronic liar and was generally disliked by his shipmates.

This patient was an only child and was reared in an economically comfortable home. He described his mother as a grouchy woman who screamed and yelled a good deal. For many years she complained of arthritis and blamed the patient for her illness because she had once fallen while bringing him lunch. Early memories of his mother reflected his hostility toward her. He recalled that she would destroy his favorite toys as means of punishment and she would state, "You broke something of mine so I will break something of yours." At other times she would tantalize him with a toy and say that it had been for him, but because he hadn't been good she would withhold it and give it to another child. The patient stated that he was never close to his mother and that he deliberately aggravated or provoked her anger. He said that she hid behind her arthritis. There was reason to believe that the mother openly encouraged or sanctioned dissocial behavior especially stealing by her son as hostile action against her husband. The father was described as a passive shy man who worked as a government financial investigator for many years. The patient's father stressed honesty and frequently related tales about people in the government who had stolen but were caught through his investigations. At the age of 15 the patient ran away from home and spent several weeks in a detention home. He enjoyed reckless activities and engaged in frequent heterosexual acts which were apparently an expression of hostility toward women. Prior to enlistment he had many hobbies and his room was always filled with hundreds of articles such as magazines, model ships, and baseball bats.

Examination of mental status revealed this patient to be of better than average intelligence. He was a fluent speaker who thought he could talk his way out of any situation. When confronted by an anxiety provoking situation he would usually withdraw or escape from it. There was evident emotional flattening and he faced life situations with a detached and distant attitude. Throughout his hospitalization he remained in a locked ward and greatly resisted any effort to be placed on an open ward. While on the locked ward he felt no anxiety and did not react. In therapy he was very resistant to any insight and was considered to represent a limited psychogenic reaction. After two months of hospitalization he was honorably discharged as unsuitable for military service.

C 4 An unmarried Navy seaman was referred for psychiatric consultation after he admitted to the theft of money from the wallets of two men in his outfit. He further stated that he had stolen considerable sums of money and clothing throughout his enlistment. He was awarded a Special Court martial and I was requested to examine him and testify at his court martial. On the basis of psychiatric opinion he was then hospitalized.

This individual began stealing shortly before enlistment when he removed hubcaps from an automobile. After enlistment he frequently stole items of clothing that usually did not fit and were not useful to him. Following the death of his father one year prior to hospitalization the patient began to steal money ostensibly because his family was then short of funds. In almost every instance the theft occurred after he had been in bed about 30 minutes and was in the twilight stage of sleep. He would then get out of bed walk through the barracks or compartments and rummage through the personal effects of others until he could find money. On one occasion he took a wallet out of the hand of a sleeping sailor but he usually removed the money from trousers hung over the bunks. Following the theft he would return to bed and on awakening in the morning realized the possession of stolen money but could not recall from whom or where the money was stolen.

The patient is the oldest of three children. As a child he did his best to provoke and aggravate his father and as a result was constantly in trouble. He would then make up a lie that his mother "always believed" and she in turn would then protect him from a spanking by his father. As a child he often felt lonely and unwanted in spite of the fact that he was given an excess of material things by his parents. Although the family was well off financially his parents would remind him of the sacrifice made each time a gift was presented. The patient's father was a highly respected individual who participated in many community functions and constantly preached against dishonesty. The patient's mother was chronically ill and controlled the family by fluctuations in her symptoms.

Psychiatric examination found this individual to be an alert and intelligent person whose greatest strength was in his glibness and his ability to outtalk his opponents. He had great dependency needs, suffered from extreme loneliness, and when alone or without activity to occupy his thoughts became very tense. The patient was hospitalized two months and responded well to therapy. He achieved considerable insight and control over his impulse to steal. Following psychotherapy the charges against him were dropped and he was honorably separated from the Navy.

Each of the four patients with kleptomania whose case histories have been presented had a perfectionistic parent who exercised rigid control and demanded honesty and social compliance from the child. The other parent was permissive or even openly sanctioned the child's antisocial behavior as a hostile act against the spouse. In each case the father was the scrupulously honest parent who was embarrassed by the child's stealing. The mother encouraged stealing by such action as repeatedly calling the child a thief, protecting him from punishment after he had stolen, accepting stolen goods as gifts, and even evincing pleasure when the child had committed a theft.

The causes of antisocial behavior were extensively studied by Johnson and Szurek.<sup>3</sup> They clearly demonstrated that repeated



stealing as well as other forms of unlawful and socially unacceptable behavior is generated by unconscious and occasionally conscious antisocial impulses in the parents. They further pointed out that parents of the nongang member delinquent child derive unconscious gratification from the child's antisocial activities. Parental fostering of antisocial behavior is believed to be a basis of the stealing pattern exhibited by each of the four patients presented. Karpman referred to Stekel's thesis which described the sexual implications frequently observed in this condition where an individual experiences an orgasm following a theft. The presence of emotions such as excitement or tension and release suggest a sexual gratification derived from the act of stealing.

Kleptomania is considered to be a symptom of a neurosis or psychosis. These patients display numerous manifestations of emotional disturbance such as severe anxiety attacks, dissociative reactions, depression, and occasionally an escape from reality. Where true kleptomania exists, it may be stated first that the act is part of a repeated psychoneurotic pattern, second that the accused exhibited mounting tension or anxiety which was relieved by the theft, and third that the act generated by the illness was so strong that the deed would have been committed even though detection was likely at the time of the offense. If these criteria are met, it is then agreed that the accused suffers from irresistible compulsion and was unable to adhere to the right. Karpman further pointed out that punishment has no deterrent effect in these cases because it does not alter the psychologic mechanisms responsible for the offenders' antisocial performances.

### SUMMARY

Kleptomania is a condition characterized by repeated episodes of nonpredatory stealing that are the result of strong unconscious forces compelling the individual to commit the offenses. Psychiatrists are frequently requested to decide whether or not an individual represents a case of kleptomania. Case histories of four persons suffering from this condition have been presented to illustrate the basic characteristics of the illness. In each case, unconscious sanctions on the part of the parents were instrumental in creating the need to steal. Psychiatric opinion holds that persons suffering from kleptomania are mentally ill and cannot be considered as criminally responsible for their crimes.

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# FABRICATION OF A RESILIENT PLASTIC INTERDENTAL SPLINT

## A Point on Technic

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**T**O PROTECT their teeth and jaws against injury during athletic events, boxers, some football players, and other athletes wear a standard rubber mouthpiece. Although this appliance affords some protection it has serious shortcomings namely (1) poor retention with resultant ease of dislodgment (2) impairment of breathing, (3) discomfort to the wearer because of unequal stresses on the teeth and excessive bulk, (4) increased muscular distress and the possibility of damage to the temporomandibular articulation because of increased vertical dimension beyond tolerable limits for prolonged periods of time and (5) the impossibility of talking or of calling signals as a quarterback is required to do.

These shortcomings were eliminated in an improved interdental splint mouthpiece developed at this School by Towle and Niiranen. Made of a resilient vinyl resin, the improved appliance fits snugly against the teeth and soft tissues and therefore is not easily dislodged. At the same time the wearer can talk or call signals with but little if any, impairment of speech. The increased vertical dimension is practically nil (about 3 mm at the incisors). Because the splint permits the pressure of normal occlusion or force of a blow to be distributed equally to all the teeth its use greatly reduces the possibility of chipping or knocking out teeth. Finally it may be worn for long periods of time with comfort.

In order to fabricate the interdental splint according to the technic originally described it is necessary to use denture flasks. Nonprosthetic facilities find it difficult to obtain such flasks, however and it is not possible to construct interdental splints

in this way at all activities. The objective of this study therefore was to develop a practical method of fabricating the improved mouthpiece that would not require a wax up and the use of denture flasks. This article describes such a procedure.

## METHODS AND MATERIALS

**Alginate Impression** An alginate maxillary impression is made. A satisfactory impression must include tuberosities, frenum and muscle attachments (fig 1A) and should be free of bubbles. A plaster water wash clears the impression of saliva and mucin and an air blast is used to remove excess moisture. The cast (fig 1B) is made with the hardest stone available for example Duroc or some similar product since it must later withstand the sustained heat of curing particularly if several splints are to be made on it. Use of a vacuum apparatus to prepare the stone mix is desirable if one is available.

**Centric Relation Record** A square consisting of three thicknesses of ordinary baseplate wax is placed between the patient's teeth. The wax wafer should be large enough to provide a peripheral excess of several millimeters (fig 1C). The patient is guided into and instructed in a centric relationship so that there will be about 2 mm of wax between the closest opposing cusps. Minimum cuspal indentations are required in the wax to prevent a locking effect when the finished appliance is worn.

**Articulator Mounting** The wax periphery is left untrimmed and the tips of the mandibular cusps are reproduced by pouring a stone mix into the mandibular arch indentations in the wax wafer. This procedure provides a smooth surface around the cusps which aids in obtaining a smoothly finished splint (fig 1D). This stone cast is trimmed as desired prior to actual mounting.

Plain line nonadjustable barn door hinge type articulators are adequate as the only movement required is a centric opening and closing. It is advisable to mount the maxillary cast on the lower arm of the articulator (fig 1E) because the liquid vinyl resin that will be applied later flows quite readily. Otherwise the mounting is done in the usual manner. Dense stone is used for the mounting as well as for the casts. The articulator should be stopped or locked to prevent accidental closure beyond the distance recorded by the wax wafer.

**Fabrication** The mounted casts are dried completely in an oven below 100 C the temperature required for steam. While the casts are still hot a stiff bristled brush is employed to coat them lightly but thoroughly and smoothly with a silicone releasing agent. This agent or separating medium may be one coating of

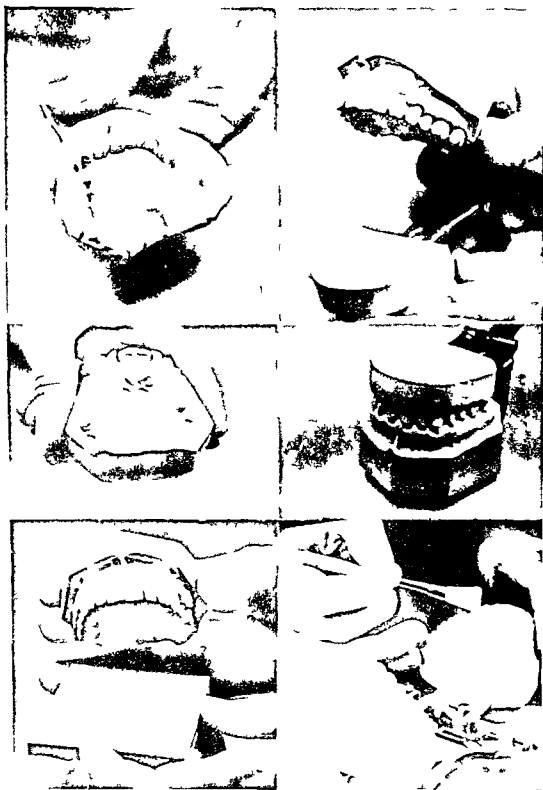


Figure 1

Mucolube (silicone releasing agent) or three coatings of a silicone paste floor wax

Camel's hair brushes of various sizes are used as indicated for different phases of the actual application of the vinyl resin. A thin layer of liquid vinyl resin is painted (fig 1F) onto the surfaces of the maxillary cast that are to be covered with the exception of the occlusal surface. To prevent flowing and puddling, thick layers should not be applied. In this respect, it is expedient to apply this and each succeeding layer by sections rather than to attempt an entire surface at one time.

The cast with this applied section of a layer is then placed in the oven at 180 C (340 F) and is allowed to remain in the oven two to three minutes or until the gloss begins to disappear from the resin. An alternate procedure is to flame the resin lightly (fig 2A). Flaming indeed is the method of choice. The best flame for the purpose seems to be provided by a hand alcohol torch. However, other flames such as from a Bunsen burner or a casting torch may be used.

Experimentation for a few minutes is recommended before attempting to flame the actual case because both the oven and the flame may result in premature curing (fig 2B). If the individual layers are overcured, the finished splint will show a laminated effect, and overcuring will usually result in separation and peeling of the various layers where the lamination shows.

Successive layers of liquid resin are applied and partially cured in this manner until all but the occlusal surface (fig 2C) is covered by the desired thickness of resin. The margins of the external and internal surfaces are extended occlusally to form the boxed-in effect of an occlusal trough (fig 2D). The extent of these marginal rims must be determined by visual inspection and test closings of the articulator. At this time an extremely thin coating of liquid resin is carefully applied to the entire external and internal surfaces and is then oven heated or flamed to produce the final smooth surface.

Throughout the above procedure, each layer should be allowed to cool before proceeding; otherwise, the next layer will start to cure as it is applied, and premature curing will result in possible entrapment of air bubbles or a grainy undesirable appearance. The occlusal trough is filled by simply pouring in liquid vinyl resin (fig 2E). Then the articulator is closed to the predetermined position. The mandibular cast cusps are now in uncured resin with the maxillary cast below (fig 2F). The case is placed in an oven at 180 C for 15 to 20 minutes until the desired cure indicated by the degree of brownness (fig 3A) is attained. The oven should be large enough so that the case does not come into contact with or come close to the sides of the oven during curing.



Figure 2

Finish After cooling, the cured splint is removed from the cast (fig 3B) and the peripheral borders are trimmed with sharp scissors to the desired dimensions. The cut edges are smoothed

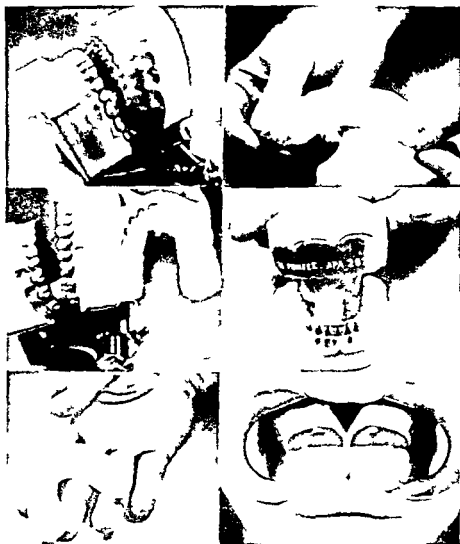


Figure 3

and rounded by carefully applying with a brush liquid vinyl resin to adjacent sections approximately an inch at a time (fig 3C) Each of these sectional applications is successively flame-cured to the same color as the rest of the splint If further curing is desirable the splint is placed on several layers of gauze or on a piece of abestos and put in the oven for the required additional length of time

Individualization of Splints This can be achieved by any one of several methods

(1) The lettering of name, date, activity, and so forth can be applied either with India ink or with various colored plastic inks on any smooth surface of the splint. This surface is then covered by a veneer of liquid vinyl resin and flamed lightly prior to the final oven cure (fig. 3D).

(2) Polyvinyl chloride resin is prepared commercially in several basic colors, and each of these can be blended or modified with pigments prepared by the manufacturers. Color may be applied by brush in any desired pattern and then veneered with an additional layer of the liquid vinyl resin.

(3) Lettering also may be applied to the flamed pigmented layer (fig. 3E) before application of the final veneer. In this way, date of splint fabrication can be noted for durability and wear records. The name of the person wearing the splint and his activity, ship, or team also can be incorporated. Team or individual colors can be utilized both for decorative purposes (fig. 3F) and as an aid in preventing dressing room mix ups of mouthpieces.

## DISCUSSION

Both the flask and paint on techniques for fabrication of resilient plastic, protective interdental splints appear to produce mouth pieces far superior to obtainable stock appliances. However, the need for flasks limits the number of activities capable of utilizing the flask technique. The paint on technique by eliminating wax up and flasking procedures, should make it possible for all facilities to provide more persons with individually constructed splints.

While it is true that with the flask technique, the operator is free to carry out other tasks while stone is setting in the flask, no appreciable deleterious effect is likely to be noted in the finished appliance if the paint on technique is interrupted from time to time for periods of one or more hours. Lettering and coloring, if desired, are applied successfully with the paint on method. Several splints can be made from each cast to provide a person with spare appliances. As with the flask technique, a smoothly rounded peripheral border is obtainable with the paint on technique.

It is believed that more research and experimentation would be advantageous and productive.

## SUMMARY

The construction of resilient plastic, interdental splints can be accomplished with the paint on technique—eliminating the



need for a wax up obviating the use of denture flasks and permitting the fabrication of such appliances at facilities lacking access to prosthetic equipment. The technic consists of painting liquid vinyl resin on a cast which has been lubricated with a silicone releasing agent as a separating medium. When the case has been built up as desired it is cured in a dry heat oven for about 20 minutes at 180 C. Individualization of splints is achieved by applying pigments for coloring or by lettering for record purposes and as a means of identification. Several splints can be constructed on each cast providing the patient with spare appliances. Splints prepared with the paint on technic appear to be as successful and as satisfactory as those produced with the flash technic and both methods apparently produce splints that are far superior to available stock appliances.

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### HEALTH A FULL TIME HOBBY

It comes as no news to physicians that something has happened to the American public in the past 20 years. People know more about their bodies and the ills that flesh is heir to than anyone would once have dreamed.

This is not to suggest that they understand physiology or that they really care about the difference between a strain and a sprain, but they do hear in a flood of new advances in diagnosis and therapy.

One thing is certain: the mass communications media have provided the public's appetite for medical news and opinion to be insatiable.

Government too has participated in the dissemination of medical news and since the thirties we have seen the tremendous development of public relations on the governmental level.

—HENRY S. M. NEIL

*Journal of Subcutaneous Medicine and Allergy*  
p. 258, July 1957

# ACUTE RHEUMATIC FEVER

## Electrocardiographic Effects of Sodium Lactate and Potassium Chloride

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**D**ISTURBANCES in rhythm and A V conduction are commonly observed in acute rheumatic fever. Both rhythm and conduction can be influenced by change in position,<sup>1-3</sup> vagal blocking agents, Mecholyl Chloride (brand of methacholine chloride),<sup>4-6</sup> and drug induced tachycardia.<sup>7</sup> Some believe that the impaired A V conduction of acute rheumatic fever, which most often is manifested by prolongation of the P R interval, is due to increased vagal tone.<sup>7</sup> As Grant<sup>8</sup> recently has pointed out, however, this explanation is doubtful because of the absence of other manifestations of vagotonia in rheumatic fever and the failure to induce P R interval prolongation by guarded stimulation or by cholinergic drugs.

The ease with which impulse generation and conduction can be influenced in rheumatic fever, as well as other cardiac disturbances<sup>9-11</sup> suggests that pH and electrolyte concentration of extracellular and intracellular fluid may be important factors through which the effects of these diverse agents may be mediated. Accordingly, the electrocardiographic effects of rapidly administered molar sodium lactate or potassium chloride or both were observed in Navy recruits ill with or convalescing from acute rheumatic fever, in the hope that an exaggerated response would be helpful in predicting those whose recovery would be delayed or who were liable to relapse after return to duty. The fact that the average period of hospitalization was 104 days<sup>12</sup> and that up to 20 per cent of those returned to active duty have a relapse serves to emphasize the importance of rheumatic fever to the Armed Forces.

### MATERIALS AND METHODS

Twenty two male patients aged 17 to 24 years, under treatment for acute rheumatic fever as established by Jones<sup>13</sup> criteria, were selected for study. Five had had previous attacks of rheumatic

fever including two with two previous episodes. Two additional patients, one with rheumatic heart disease with 2:1 A-V block and one with complete A-V block due to arteriosclerotic heart disease, also were studied. The majority of rheumatic fever subjects received aspirin, cortisone, or both during the period of study; the nonrheumatic subjects received no therapy. All subjects demonstrated some type of ECG abnormality at some time during their illness, but not necessarily at the time of study.

The interval that elapsed between onset of disease and investigation varied from two to seven days in all except two individuals who were studied during the second and fourth week of their illness while the disease was still active. Five subjects were studied on two occasions. In most cases the studies were carried out at least two hours after eating, but no special effort was made to ensure a uniform time interval with respect to meals for the group as a whole. Normal renal function was present in all subjects.

A routine 12-lead ECG was obtained on each subject shortly after admission to the hospital, and therefore any anxiety connected with this procedure could be expected to be less on a subsequent occasion. The three standard limb leads were recorded as a base line and, unless otherwise noted, only lead II was obtained during the study. Blood for serum sodium and potassium was obtained before and immediately after the infusion.

**Sodium Lactate.** Eleven subjects with acute rheumatic fever received 200 mEq of 1 molar sodium lactate intravenously within 5 to 10 minutes, and 2 of the 11 received an additional 200 mEq on a second occasion. The same material was given to 2 subjects with the following conditions: inactive rheumatic heart disease with complete A-V block and arteriosclerotic heart disease with 2:1 A-V block.

**Potassium Chloride.** Ten subjects received 40 mEq of KCl dissolved in 1,000 ml of 5 per cent *d*-glucose solution intravenously within 40 to 60 minutes. Six additional patients received this solution immediately following the infusion of 200 mEq of sodium lactate.

## RESULTS

**Sodium Lactate Side Effects.** Symptoms and signs of tetany appeared in every subject, usually after the first 100 mEq of lactate was infused. Numbness, tingling, and muscle cramps appeared regularly. Chvostek's sign was elicited only occasionally. In no case were the side effects sufficiently distressing to interrupt the infusion, and they disappeared within a few minutes after infusion was completed.

**Potassium Chloride Side Effects** Pain believed to be of venous origin, appeared in the elbow, arm, or shoulder of all those who were given KCl, with one exception. In two subjects not included in this study, the pain was severe enough to make it necessary to discontinue the infusion. Pain, and occasionally tenderness, persisted in the involved area for an hour or more but no other objective evidence of thrombophlebitis or thrombosis appeared.

**Serum Sodium and Potassium** As shown in table 1, there was no significant change in the serum concentration of either sodium or potassium. The data indicate that KCl tended to reduce serum sodium whether or not sodium lactate was given first. In 7 of 20 subjects, there was a fall in serum sodium of 10 mEq/l or greater, the maximum fall being 17.5 mEq/l. Serum potassium was significantly elevated only when KCl was given alone, the maximum rise being 1.9 mEq/l.

**Significant ECG Effects** In subjects with sinus rhythm the P-R interval remained unchanged. As shown in table 1 and the subsequent figures, T wave amplitude decreased but only rarely did T become negative. The Q-T<sub>c</sub> interval was regularly prolonged. In two patients with interference dissociation, lactate restored the rhythm to normal sinus rhythm (fig. 1).

Figures 2 and 3 illustrate two examples of a shifting pacemaker. While no effect on rhythm or A-V conduction was observed

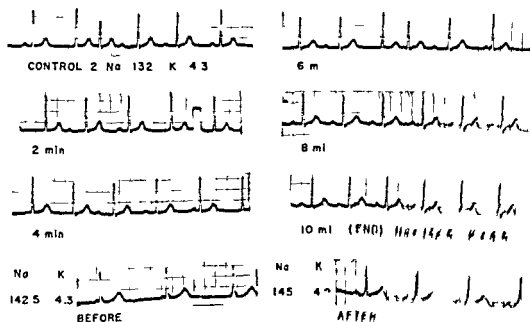


Figure 1 The effect of molar lactate infusion (10 ml) on the patient with acute rheumatic fever showing interference dissociation on the electrocardiogram. The upper three strips of each column are for the same individual and the lower two are those of another individual before and after the infusion. Note change in rhythm from interference dissociation to sinus rhythm.

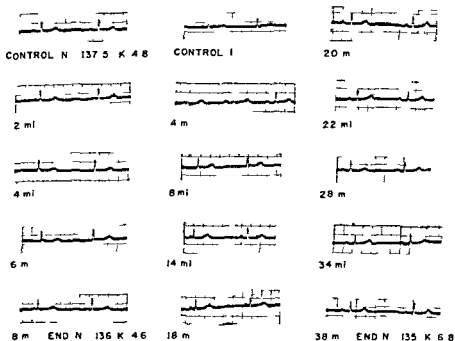


Fig 2 Example of heart g p emake ult ng from f o f m l l a t a d to at n to co trol t t by KCL Th arl chang the f st f w m t of KCL adm st t o ar probably t l l d to the lact te f o ( t xt)

in the 24 year old subject with inactive rheumatic heart disease and complete A V block aggravation of A V conduction did occur in the 45 year old subject with arteriosclerotic heart disease (fig 4). In this case the 2:1 block observed in the control tracing changed to temporary complete block during the infusion and later reverted to the control status. The atrial rate increased from 80 to 100 per min (table 1) whereas the ventricular rate increased from 40 to 43 per min.

As shown in table 1 and in figure 5, KCl administration produced a striking reduction in P wave amplitude while the P R interval remained unchanged with one exception. In this instance (fig 6) the P R interval intermittently varied from 0.20 seconds to 0.28 seconds without a significant change in heart rate. There was no effect on P P interval when the study was repeated using 40 mEq of NaCl on the following day. The difficulty in measuring P R interval when a portion of P may be isoelectric is obvious so that A V conduction cannot really be evaluated.

The effect of KCl on P wave amplitude varied depending on whether it was given alone or immediately following lactate. In the former case a significant decrease occurred but there was no significant change when KCl followed sodium lactate. Figure 4

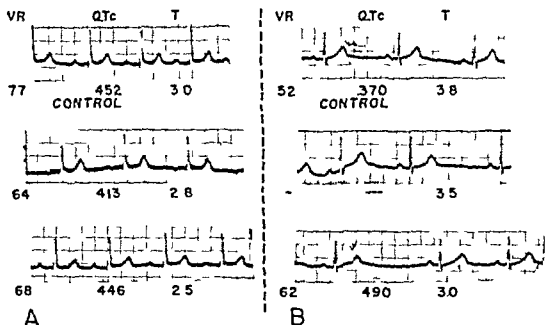


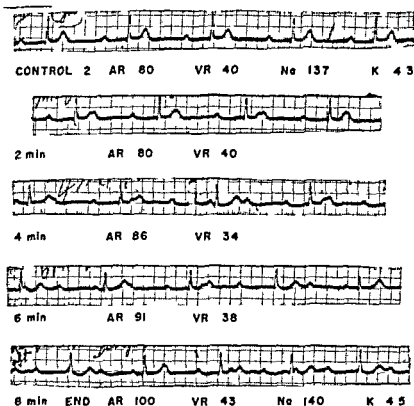
Figure 3 Another example of shifting pacemaker (A) (sinus to nodal) resulting from lactate administration. The change in rhythm was temporary but on return to a sinus pacemaker the prolonged P R interval persisted. The effect of lactate on Q-Tc interval T and rhythm regularity (B). The Q-Tc interval is considerably prolonged T decreased in amplitude and the rhythm markedly irregular. The arrow in the lower strip points to a blocked P wave that arrived during the refractory state.

shows how KCl induced intermittent first degree A V block that could not be reproduced by NaCl in the same concentration on the following day.

The arrhythmia induced by lactate administration often was restored to its former state by subsequent KCl administration (fig. 2). In contrast to the effect of sodium lactate, T wave amplitude greatly increased following KCl infusion and was most evident in those subjects in whom the T wave had been depressed by prior lactate administration. T wave amplitude increased 1 mm or more in 12 of 20 experiments, and in 3 subjects increased 2 mm. The Q-Tc interval itself was not significantly altered. The slowing of the ventricular rate (due to slowing the rate of discharge of impulses from the pacemaker) is evident from table 1.

#### DISCUSSION

That pH and certain electrolytes, chiefly  $K^+$ ,  $Ca^{++}$ , and  $Mg^{++}$ , influence rhythmicity and conduction of impulses in the heart has been known for many years. Sympathetic and vagal activity also are recognized as important conditioning influences. It always is difficult to evaluate a single factor because others may be changed in the process. For example the effect of the sodium lactate may be attributed more to the change in pH than to the sodium or lactate ions themselves.<sup>14-16</sup> Indeed, Bellet, Wasserman, and Brody<sup>5</sup> found no consistent alteration in serum sodium follow-



Figur 4. Th ff t f m l l t te f w a 45 y r ld m a u th a terio cl t b t a d 21 AV bl k. Th arle t ff t a c e d t th pa t f alt at P w f m th T u av bouever corpl t l v d o t n l t nat ly de l ped.

in lactate administration but regularly found a fall in serum potassium. As also noted by others, however, no correlation was found between serum electrolytes and ECC changes.

The failure to demonstrate a significant fall in serum potassium following lactate administration in this study may be attributed to the early timing of sampling. The maximum drop in serum potassium occurs one hour after lactate administration. This explanation might also apply to different effects on P wave amplitude that were noted. When the drugs were given in sequence the depressant effect of ICl on P wave amplitude was probably counteracted by the opposite effect of the prior lactate administration. Bollet and associates found no significant drop in total serum Ca with lactate administration, but the ionizable fraction was not determined.

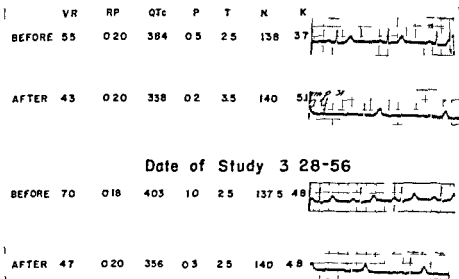
The most interesting results of this study were those involving A V conduction or rhythm changes. In general, A V conduction was accelerated by sodium lactate, but on one occasion > 1 A V

TABLE 1 Serum electrolyte values and electrocardiographic measurements after intravenous administration of sodium lactate and potassium chloride

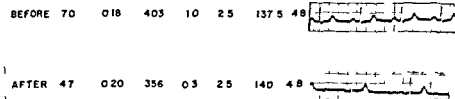
	Na lactate				KCl alone				KCl following Na lactate			
	Before		After		Before		After		Before		After	
	N	t	N	t	N	t	N	t	N	t	N	t
Na (mEq/l)	12	134.5	136.5	0.93	10	139.5	135.3	1.88	8	137.5	130.0	1.58
K (mEq/l)	12	4.6	4.6	1.40	12	4.5	5.1	2.02	7	4.6	4.7	1.74
P (mm)	12	-	-	-	12	0.84	0.56	2.49	7	0.33	0.47	1.03
P R (sec)	9	0.22	0.20	1.77	11	0.17	0.18	-	7	0.22	0.3	0.11
T (mm)	12	2.3	1.7	2.50	13	2.60	3.35	2.27	5	1.5	0.4	1.1
QTc (sec)	11	0.415	0.457	2.25	10	0.412	0.411	-	7	0.435	0.4	1.1
QTc - (sec. min.)	-	-	-	-	17	0.415	0.411	1.0	-	-	-	-

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## Date of Study 3 28-56



Figur 5 The effect of KCl infusion on P and T wave amplitude on the same individual studied on two different occasions. Slowing of the heart rate may be noted.

block was changed to complete block. This change was associated with a moderate increase in atrial rate (from 80 per min to 100 per min) but with little increase in ventricular rate (from 40 per min to 43 per min). This is of special interest because lactate is currently recommended for use in complete block with slow ventricular rate.

In this connection Scherf, Goldfarb, and Bussan<sup>9</sup> found that paroxysmal tachycardia of apical or ventricular origin temporarily disappeared with hyperventilation. They believed that alkalosis was responsible. The opposite effect, that of acute respiratory acidosis produced by administering 30 per cent carbon dioxide to mentally disturbed patients, resulted in a high incidence of atrial and ventricular irritability with the production of ectopic beats and bursts of tachycardia.

Certain well known effects of KCl administration were readily noted in this study—decrease in P wave amplitude, slowing of the heart rate, and increase in T wave amplitude. No untoward effect on rhythm or ventricular conduction was noted when KCl was given rapidly to patients with acute rheumatic fever and normal renal function. In only one subject was intermittent P-R interval prolongation noted during the KCl infusion. In fact, in several instances of arrhythmia induced by sodium lactate, the administration of KCl restored the rhythm to its previous state.

The KCl study was planned initially as a possible means of predicting relapses in rheumatic fever. Had it been possible to

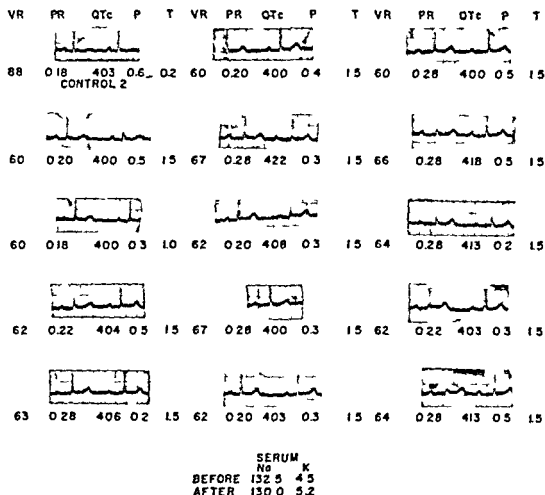


Figure 6. Intermittent first degree A-V block produced by KCl infusion. This is the only instance of P-R interval prolongation noted with KCl. The usual effects on P- and T-wave amplitude and heart rate are conspicuously absent. The study repeated on the following day using NaCl in the same concentration in place of KCl had no effect (ECG not shown).

single out the relapse-prone individuals by demonstrating in them an exaggerated response to KCl, a potential toxic agent, then such subjects could be maintained under treatment for a longer period and be retested periodically. The value of this test has not as yet been demonstrated by follow-up data, and more information is necessary. Inasmuch as up to 20 per cent of those returned to duty may relapse, such a prognostic aid would be very useful.

### SUMMARY

The acute effects of rapidly administered one molar sodium lactate (200 mEq in 8 to 10 min) or KCl (40 mEq in 40 to 60 min) or a combination of the two, were observed in young men ill with or convalescing from acute rheumatic fever. Most showed some FCC abnormality during the course of their disease. Sodium lactate did influence rhythmicity in 50 per cent of the subjects

and temporarily restored interference dissociation to sinus rhythm in two patients. Potassium chloride only occasionally affected rhythmicity out regularly affected P and T wave amplitudes. Electrocardiographic effects could not be correlated with serum sodium or potassium changes. The response to either lactate or KCl administration for use as a prognostic aid in predicting the time required for recovery or relapse rate has not yet been evaluated.

ACKNOWLEDGMENT I w h t th k D R h d E B t s fo fe ing  
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# PORTAL CIRRHOSIS

## A Study of 100 Consecutive Autopsied Cases

MICHAEL D DAVIS M D

**T**HIS report concerns 100 consecutive cases of cirrhosis of the liver in which autopsies were performed at this hospital between 1949 and 1956. Only the Laennec and post necrotic types were included, excluding various types of obstructive cirrhosis. Many aspects of these cases were studied including age, cause of death, presence of hepatomegaly and splenomegaly, incidence of complications that were direct results of the liver disease, such as esophageal varices, esophageal and gastric hemorrhage, icterus, ascites, anasarca, hepatoma, biliary tract disease, acute tubular necrosis, hyperplasia of the prostate and testicular atrophy, and incidence of incidental pathology that probably was not related to the liver disease, such as peptic ulcer, cardiovascular diseases, renal diseases, various infectious diseases, and malignant tumors not primary of the liver.

These findings are presented as observations and speculations as to the relationships of diseases associated with cirrhosis will be kept to a minimum. It is well known that some conditions, such as esophageal varices, are obviously and directly associated with cirrhosis. Others, such as hepatoma and hyperplasia of the prostate gland, probably are related to cirrhosis, although not in so obvious a fashion. Still others, such as cardiovascular diseases, apparently are not related except that their incidence is decreased in liver disease.

The cases in this series, which was restricted to the so called portal or diffuse nodular cirrhosis, were divided into (1) the common finely nodular type, referred to as Laennec's or alcoholic cirrhosis, of which there were 88 cases, and the postnecrotic type, of which there were 12. The groups were identified by these criteria: (1) history of alcoholism, (2) history of hepatitis, (3) gross appearance of the liver, and (4) microscopic appearance of the liver.

It is realized that perhaps the criteria are over simplified and that clinicians often use other observations for differentiating

F m U S V t      Admin str t      H p t l C r l G bl      Fla. Dr. Da      i n w  
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the two types of cirrhosis. In fact considerable difficulty was encountered in separating the two groups. The extent or even the presence of alcoholism and nutritional deficiency as judged from the history alone often is impossible to assess. The attack of hepatitis may have taken place as long as 30 years previously. It may have been forgotten or misdiagnosed or have been anicteric or subclinical. There is no reason why a chronic alcoholic may not contract hepatitis nor why a hepatitis victim may not prior to or after his infectious disease develop chronic alcoholism.

In assessing these cases in retrospect it was found that the gross and microscopic picture of the liver was the only reasonably accurate method of differentiation and even this was beset by many errors. In fact many authorities refuse to place much credence on such physical observations and the statement often is made that both types of cirrhosis if they progress to their inexorable conclusion result in a shrunken scarred and atrophic liver at which stage the causative agents and course can only be guessed at.<sup>14</sup>

In this study relatively finely nodular livers with pseudolobules that were diffusely distributed and outlined by relatively narrow zones of fibrous tissue and often showing fat vacuoles in the liver cells were designated as the Laennec type. Conversely the coarsely nodular livers with pseudolobules scattered in irregular distribution and outlined by relatively abundant connective tissue and with no fat in the liver cells were considered to be of the postnecrotic type.

It is obvious that the number of cases of postnecrotic cirrhosis was too small for the findings to be statistically significant. Apparently other institutions have a similar dearth of postnecrotic cirrhosis cases. The largest published series included only 43 cases.<sup>1</sup> In regard to a few aspects however a comparison may be interesting or even significant. Age of death in patients with cirrhosis is shown in table 1. Our data correspond to other reported series which indicated that cirrhosis has a peak incidence during middle age. In most series however postnecrotic cirrhosis appears to have involved a younger age group in both its inception and its fatal terminations than was found in our series. Of more interest and importance would be the average and mean age at onset of the disease and the length of survival after onset but this information was not available in a large number of cases.

TABLE 1 Age distribution 100 cases of portal cirrhosis by type

Type	Number of	Number under 40 years	Age group	Range in years
L	88	7	52-9	31-78
P	12	1	58-0	27-78

Causes of death are listed in table 2 according to what was considered to be the immediate cause. Here again there was some difficulty in judgment. In most cases the cirrhosis was severe enough to contribute actively to the patient's death. Eighty one per cent of the patients with Laennec's cirrhosis and 83 per cent of those with postnecrotic cirrhosis died as a result of hepatic failure or hemorrhages from esophageal varices which are the usual causes of death in these cases. A few developed fatal hepatorenal syndrome or hepatoma which may or may not be considered direct derivatives of hepatic cirrhosis. The remainder died from unrelated causes, and in a number of cases the diagnosis of cirrhosis was made only at autopsy. Approximately 10 per cent of our patients with Laennec's cirrhosis although exhibiting definite cirrhosis at autopsy, did not develop sufficient signs or symptoms to lead to suspicion of cirrhosis clinically. In a few, signs of cirrhosis were masked or confused by the presence of other diseases.

TABLE 2 *Immediate cause of death in 100 patients with portal cirrhosis*

Immediate cause of death	Laennec's cirrhosis		Postnecrotic cirrhosis	
	Number	Per cent	Number	Per cent
Hepatic failure	47	53.4	7	58.3
Hemorrhage esophageal varices	24	27.3	3	25.0
Hemorrhage duodenal ulcer	2	2.3		
Hepatorenal syndrome	5	5.7		
Cardiac disease	4	4.5	2	16.7
Carcinoma	3	3.4		
Acute pancreatic necrosis	2	2.3		
Trauma	1	1.1		
Total	88	100.0	12	100.0

In this study the cause of death did not differ significantly between Laennec's and postnecrotic cirrhosis. Over half of both types of patients died in hepatic failure and about one fourth were exsanguinated from varices of the esophagus.

As shown in table 3 the liver at time of death tended to weigh more than normal. In other words most of the deaths occurred well before the stage of atrophic shrunken liver had been reached. In the Laennec cases the excessive weight was due to abundance of fat; these livers were invariably enlarged in dimensions as well as in weight. The increased weight of the liver in postnecrotic cases was due to increased scar tissue and the weight bore no relation to the size. In fact, most such livers were relatively small in size. A greater proportion of livers of patients

with postnecrotic cirrhosis were of abnormally low weight as well as of small size than were the livers of patients with Laennec's cirrhosis

TABLE 3 Weight of liver 100 s / p tal rrb

Type of cirrhosis	Number of cases	Over 1700 g	Under 1300 g	Average weight in g	Range of weight in g
Laennec's	88	60	12	2276	1050-5000
Postnecrotic	12	6	4	1920	950-3250

The average weight of spleens in our cirrhosis cases as can be seen in table 4 was considerably increased using 300 grams as the upper limit of normal. The average weight was greater in postnecrotic cirrhosis than in Laennec's cirrhosis but the range from minimum to maximum was considerably greater in Laennec's cirrhosis as would be expected from the larger number of cases. In a few instances spleens were under 100 grams in weight. These can be explained only by postulating the presence of anomalous or damaged splenic venous circulation. The series reported by Baggenstoss and Stauffer<sup>3</sup> showed similar findings with 67 per cent splenomegaly in postnecrotic cases and 80 per cent in Laennec's cirrhosis. Most series have shown an increased incidence of splenomegaly in Laennec's over postnecrotic cirrhosis. The reasons for this have never been explained. Some studies seem to indicate that splenomegaly increases in incidence with the duration of the cirrhosis and that shrunken atrophic livers are more apt to be associated with very large spleens.

TABLE 4 Weight of spleen 100 s / p tal rrb

Type of cirrhosis	Number of cases	Over 300 g	Average weight in g	Range of weight in g
Laennec's	88	66	367	60-1200
Postnecrotic	12	8	435	250-755

Our study suggests that patients with postnecrotic cirrhosis are more prone to develop esophageal varices but are less apt to bleed from them (table 5). This is in contrast to most of the prior studies which have shown a greater incidence of varices as well as of hemorrhages in Laennec's cirrhosis. Baggenstoss and Stauffer found that 75 per cent of their patients with Laennec's cirrhosis had varices and 27 per cent hemorrhaged of their postnecrotic cases only 37 per cent had varices and 16 per cent hemorrhaged. Our series is in agreement with others in showing that patients with postnecrotic cirrhosis are less prone to develop significant esophageal bleeding. The reason for this is undetermined.

TABLE 5 *Incidence of esophageal varices in 100 cases of portal cirrhosis*

Type of cirrhosis	Number of cases	Number of varices	Number with hemorrhage	Number without hemorrhage
Laennec's	88	57	36	21
Postnecrotic	12	9	3	6
Total	100	66	39	27

The incidence of peptic ulcer in cirrhotics has been investigated extensively and much has been written about it. Most authorities agree that acute peptic ulcer appears to be entirely unrelated to cirrhosis but that the incidence of chronic peptic ulcer is increased in portal cirrhosis. As shown in table 6, chronic ulcer was present in 8 of the 100 cases in our series. Palmer and Brick<sup>4</sup> in a series of 150 cases, found 10 with peptic ulcer, an incidence of 7 per cent. In 302 cases of cirrhosis, Lipp and Lipsitz<sup>5</sup> found 5 per cent with active chronic ulcer and 11.5 per cent with scars from healed ulcers. Autopsy studies showed that 33 per cent had some form of gastric lesion other than ulcer, chiefly gastritis. Schnitzer and Hass<sup>6</sup> reported a 19.5 per cent ulcer incidence in cirrhotics.

TABLE 6 *Incidence of peptic ulcer in 100 cases of portal cirrhosis*

Type of cirrhosis	Number of cases	Number of ulcers	Gastric ulcer		Duodenal ulcer	
			Chronic	Acute	Chronic	Acute
Laennec's	88	11	3	1	4	3
Postnecrotic	12	3	—	1	1	1
Total	100	14	3	2	5	4

Cause and effect relationship between cirrhosis and ulcer are obscure. It has been shown many times that liver function often is impaired in patients with chronic peptic ulcer as revealed by laboratory tests. It has been the experience at this hospital that many deaths following gastric resection for ulcer have been at least in part due to liver disease, chiefly fatty metamorphosis. Statistics in regard to this have not been tabulated. Some writers have stated that cirrhosis predisposes to peptic ulcer, possibly because of vitamin A deficiency or hypoglycemia with gastric hypersecretion.<sup>7</sup> Our figure of 8 per cent of cirrhosis patients with chronic ulcer is considerably greater than the ulcer incidence found in other series of 100 consecutive autopsies and in con-



secutive series of other diseases such as cardiovascular disease or carcinoma

Chronic gallbladder disease including cholecystitis cholelithiasis or a combination of the two is shown in table 7 Cholecystitis with or without calculi was listed separately from cholelithiasis in the absence of detectable inflammation Type of calculi was not studied Other series studied have shown similar findings In fact a series of 500 cases of cirrhosis reported by Bucalo showed 13.6 per cent with gallbladder calculi as compared with 13.2 per cent in normal control series

TABLE 7 Incidence of gallbladder and pancreas 100 cases of postnecrotic cirrhosis

Type of cirrhosis	Number of	Cholecystitis	Cholelithiasis	Fibrosis of pancreas	Number of pancreas
Latent Postnecrotic	88 12	5 1	12 1	11 3	3 —
Total	100	6	13	14	3

In this series 14.0 per cent of the cases showed fibrosis of the pancreas This lesion has been mentioned prominently for many years as associated with cirrhosis In most cases clinical evidence of pancreatic insufficiency has been masked by the cirrhosis and the pancreatic fibrosis has been found only at autopsy It is widely thought that the same factor probably causes both hepatic and pancreatic disease

In our series carcinoma excluding hepatoma does not appear to have any significant relationship to cirrhosis (table 8) Many studies have been made in an attempt to establish a positive or negative correlation between cirrhosis and malignant disease Theoretically the presence of disturbances in steroid metabolism in cirrhosis should predispose to several types of malignancy but the studies have shown wide variation and do not appear to establish any relationship It has long been known that hepatoma often is associated with cirrhosis Of interest is the 4 cases of hepatoma seen in our 12 cases of postnecrotic cirrhosis This high incidence has been noted in other series

TABLE 8 Carcinoma associated with postnecrotic cirrhosis 100

Type of tumor	Number of	Liver	Pancreas (latency)	Larynx	Intestine (mouth)	Stomach	Colon	Endometrium	Ectocervix
Liver tumor	8	5	2	1		2	1	0	0
Other				2	2	2			1

Cardiovascular diseases chiefly arteriosclerotic have long been known to occur with decreased frequency in cirrhosis.<sup>11</sup> In this series, only one patient developed an acute coronary thrombosis (table 9). Twenty nine per cent of our patients showed old myocardial scars. This is roughly comparable with noncirrhotic patients of similar age groups. There is a striking paucity of cerebrovascular disease (2 per cent) when we consider the age group with which we are dealing. Likewise the presence of systemic hypertension, with an incidence of 10 per cent, is low when the age group is considered. Criteria used for hypertension were blood pressure above 150 over 90 mm Hg or heart weight over 400 grams. Heart weight was used in most instances because many patients were admitted in a state of shock and their prior blood pressure was not known. Hall, Olson and Davis<sup>12</sup> in reviewing 782 autopsy protocols of patients with cirrhosis discussed this subject thoroughly.

TABLE 9 *Incidence of cardiovascular diseases in 100 cases of portal cirrhosis*

Type of cirrhosis	Number of cases	Coronary thrombosis		Cerebrovascular diseases (old)	Hypertension
		Acute	Old		
Laennec's	88	1	26	1	8
Postnecrotic	12	0	3	1	2
Total	100	1	29	2	10

There have been many speculations as to the reasons for reduced arteriosclerosis and hypertension in cirrhosis but no final or convincing answer has been presented. Theories include (1) Alcohol, itself is a vasodilator. (2) The diseased liver may release excess vasodepressor substances or may fail to inactivate them. (3) The diseased liver may fail to manufacture vasopressor substance. (4) The diseased liver may interfere with metabolism or transportation of abnormal lipid material that otherwise would play a part in the development of arteriosclerosis. (5) Dietary deficiencies concerned in the etiology of cirrhosis may impede the development of arteriosclerosis.

It would be of great interest to study a larger series of post necrotic cirrhosis cases to determine the incidence of arteriosclerotic cardiovascular disease, and thus assess the effect of alcohol and diet. One might suspect in this series that arteriosclerosis and hypertension in postnecrotic cirrhosis may approach the normal group in incidence. Our 12 cases however are too small in number to justify such a conclusion.

Incidence of the chronic renal diseases as shown by the first three listed in table 10 does not appear to be significant. A number of studies chiefly in the foreign journals describe obscure changes in the kidneys in cirrhosis none of which appear to conform to recognizable disease entities. "Acute tubular necrosis is seen in kidneys of patients in shock and hepatorenal syndromes." These entities are thought to be similar conditions the latter representing the consequence of severe or prolonged shock resulting in renal failure. Either may occur after shock resulting from hepatic failure or hemorrhage. A nephrotoxin produced by the failing liver has been postulated by some authorities as the cause of the hepatorenal syndrome but this theory is currently viewed with suspicion. The single case of bilateral cortical necrosis was regarded as coincidental.

TABLE 10 Incidence of renal diseases 100 cases of portal cirrhosis

Type of cirrhosis	Number of cases	Nephrotic	Glomerulonephritis	Pyelonephritis	N	
					Acute tubular necrosis (including hypodermic)	Bilateral cortical
L	88	13	1	2	12	1
P	12	3	0	1	1	0
Total	100	16	1	3	13	1

Testicular atrophy is well known and frequent complication of cirrhosis and occurred in 71 of our cases (table 11). This of course is much higher than in normal controls of the same age group but not much higher than in cases of cachexia due to such diseases as terminal carcinoma. It always has been assumed that testicular atrophy is caused by increased amounts of es

TABLE 11 Incidence of diseases of the genitourinary system (excluding the kidney) 100 cases of portal cirrhosis

Type of cirrhosis	Number of cases	Testicular atrophy	Hypoplasia of prostate	Carcinoma of prostate (total)
L	88	62	31	5
P	12	9	7	2
Total	100	71	38	7

trogenic hormone which is not inactivated adequately by a cirrhotic liver. It also is known, however, that similar atrophy is common in severe malnutrition, inanition and all chronic wasting diseases. No statistical comparison has ever been made of these conditions in regard to testicular atrophy.

Hyperplasia of the prostate in relation to cirrhosis has been the subject of numerous surveys.<sup>11-13</sup> These have varied widely, some showing an increased incidence of hyperplasia in cirrhosis, and others a reduced incidence. This is probably due to confusion in criteria for the diagnosis of hyperplasia of the prostate. Our series with a total of 78 per cent is somewhat low. The expected incidence in the age group investigated here (50 to 60 years) is about 50 per cent.

The 7 per cent incidence of latent carcinoma of the prostate in this series may be misleading. In most of the series that have been reported where such lesions were looked for or making a wider survey of prostatic tissue there was an incidence of 15 to 20 per cent in all patients over the age of 50. This figure has been found to hold true at this hospital when the lesion was looked for by taking numerous blocks of the prostate. However this was done in only a few cases of this series and our percentage may be too low for that reason. It has been theorized that the high estrogen level in cirrhosis may block the development of prostatic carcinoma. Statistics from other hospitals neither confirm nor deny this. Other evidence of a hyperestrogenic state in cirrhosis such as gynecomastia and skin and hair changes were not noted adequately in the autopsy protocols of these patients.

Incidence of icterus, ascites, and anasarca in this series is reported as a matter of interest but the percentages found do not appear particularly significant (table 12).

TABLE 12. Incidence of icterus, ascites, and anasarca, in 100 cases of portal cirrhosis

Type of cirrhosis	Number of cases	Icterus	Ascites	Anasarca
Laennec's	88	44	50	17
Postnecrotic	12	8	12	4
Total	100	52	62	21

Seven of the cirrhotic patients also had diabetes mellitus. Pandom sampling of autopsy protocols of patients at this hospital show that this incidence of diabetes is not significantly increased although it is well known that disturbances in carbohydrate metabolism are rather common in cirrhosis as well as in other

chronic liver diseases. It also is known that diabetes is often complicated by hepatic changes occasionally including portal cirrhosis. A number of series have been published the majority of which do not find increased incidence of diabetes in cases of cirrhosis the incidence ranging from 1 to 7.6 per cent. Several studies have shown a slightly increased incidence of cirrhosis in large groups of patients with fatal diabetes. The incidence of infections including tuberculosis was remarkably low in our group of cases (table 13). Various studies have shown a much higher incidence of infections chiefly pneumonia and peritonitis which were listed as the chief cause of death. Infectious diseases were listed as the chief cause of death in 33 per cent of the 782 cases from Los Angeles County Hospital reported on by Hall Olsen and Davis. Infection was not the cause of death in any of the patients in our series. Many cases in other series however extend back to preantibiotic days. A number of series are from large city and county hospitals where many cirrhotics were derelicts admitted in terminal condition.

TABLE 13. Miscellaneous conditions associated with 100 cases of portal cirrhosis

Type of cirrhosis	Number of cases	Diabetes mellitus	Tuberculosis (of pulmonary type)	Bronchopneumonia (including aspiration)	Apoplexy (lethal)
Laennec type	88	6	6	11	3
Postnecrotic	12	1	0	0	0
Total	100	7	6	11	3

### SUMMARY

In investigating the anatomic features and associated pathology of 100 cases of portal cirrhosis (88 of the Laennec type and 12 of postnecrotic type) it was found that in comparing Laennec's and postnecrotic cirrhosis cases about 50 per cent of both groups died in hepatic failure, 25 per cent as a result of hemorrhage from esophageal varices and 25 per cent from other cause. Postnecrotic cirrhosis was more often associated with esophageal varices but less often with hemorrhage from varices. The incidence of chronic cholecystitis, cholelithiasis and pancreatic fibrosis was increased in cirrhosis cases. The incidence of carcinoma other than hepatoma was not materially affected. Hepatoma was present in one third of all postnecrotic cirrhosis cases. The incidence of systemic hypertension and arterio-sclerotic cardiovascular disease was decreased in cirrhosis while the incidence of chronic renal disease was not affected. Testicular atrophy was increased and hyperplasia of the prostate was decreased in cirrhosis.

Postnecrotic cirrhosis patients appeared more prone to jaundice ascites, and anasarca than were Laennec's cirrhosis patients in this study Diabetes mellitus was not increased The incidence of infections of all types in this series was much lower than in most other published series of cirrhosis cases

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# INSECTICIDE RESISTANCE IN HOUSEFLIES OF JAPAN KOREA, AND THE RYUKYU ISLANDS

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THE PHENOMENON of resistance of the housefly *Musca domestica* to insecticides is now known to be of world wide occurrence. Resistance to DDT and lindane in and around U S Armed Forces installations has been suspected in Japan Korea and the Ryukyu Islands in late years but no positive experimental observations had been recorded until Evers Wheeler and Blakeslee in a series of tests conducted in 1954 1955 reported four strains of houseflies from Japan and one strain from Okinawa to be moderately resistant to one or both of these insecticides. These laboratory tests at least partially confirmed field observations in areas where variations had been encountered in the apparent susceptibility of local strains of houseflies to the killing action of members of the chlorinated hydrocarbon group of insecticides.

With the exception of Ishigaki shima Ryukyu Islands where no extensive program in the chemical control of houseflies has been carried out in past years DDT lindane, dieldrin or malathion have been used practically continuously in Japan Korea and the Ryukyu Islands since 1945 and houseflies have exhibited signs of progressively developing resistance. The study reported herein concerns the comparative susceptibility of progeny of houseflies from the localities to the insecticides mentioned.

## MATERIALS AND METHOD

A series of tests of housefly resistance to insecticides involving 13 strains of flies from Japan Korea and the Ryukyu Islands was begun in October 1955 and continued through May 1956. From October 1956 to June 1957 another series of tests was undertaken on 18 strains of flies originating on military establishments in Japan and the Ryukyu Islands or within their immediate vicinities. No strains were received from Korea in the 1956-1957 series.

The method of study was similar to that used by Byers, Wheeler, and Blakeslee. Colonies of houseflies collected from 13 areas in Japan, 6 areas in the Ryukyu Islands, and 1 area in Korea were established in the laboratory, and their progeny were employed for experimentation.

Adult flies originally obtained from each of the areas were housed in wooden bottom, frame cages 10 by 10 by 8 inches. Double walls of 18 mesh black enameled screen enclosed the cage frame on the top and on three sides. A removable stockinet entrance sleeve was attached to the unscreened side. Approximately 20 ml of whole milk was provided daily as food. "Baiting" for egg deposition was accomplished twice weekly.

Two-gallon glass animal jars, with removable cloth tops, were used as rearing chambers. Viable ova of each fly strain, in 3 ml measured amounts, were used to seed the cultures. Media in each jar consisted of 400 grams Chemical Specialty Manufacturers Association larval media, 900 ml water, 50 ml molasses, and 50 ml of a 50 per cent yeast solution. Larval cultures and adult colonies were maintained at a temperature of  $27^{\circ}\text{C} \pm 2^{\circ}\text{C}$  at approximately 70 per cent humidity. Upon reaching the last larval instar, sterilized dry sand, to a depth of 2 inches, was placed over the surface of the culture media in each jar to provide a suitable pupation site.

Pupae from each culture were divided into two lots, one lot to provide a continuous stock supply of flies, the second lot for experimental use. Stock flies were housed in screened cages. Experimental flies were housed in glass animal jars equipped with stockinet sleeves affixed over the mouth of each jar by a 1 inch band of masking tape. All cages and jars were labeled with data pertinent to the fly strain housed within.

Only adult female flies three to five days old were used in test procedures, as it had been found that males are more susceptible than females to insecticidal action. For ease of handling, experimental flies were first anesthetized within their rearing chamber with carbon dioxide gas, then transferred to a Buchner funnel and held under partial anesthesia for not more than 20 minutes. A longer period was found to be fatal to a majority of the flies.

Insecticides used in this investigation were obtained from Japanese insecticide manufacturers. A five fold dilution ratio of 625 to 0.000064 ( $6.25 \times 10^2$  to  $6.4 \times 10^{-3}$ ) micrograms of toxicant per ml of acetone for each of the four insecticides (DDT, lindane, dieldrin, and malathion) was prepared in 50-ml volumetric flasks and stored in a dark cabinet. This dilution ratio was selected as a matter of experimental convenience and to satisfy one condition of the Thompson<sup>7</sup> method, namely, that the doses of agent increase by a constant ratio.



By means of a microsyringe dispensing apparatus described by Trevan, topical applications of 2  $\mu$ l of solution for each dosage level of a given insecticide were administered to the dorsum of individual female flies in each of the test series. Acetone administered in the same manner was used in control groups.

Previously calibrated  $\frac{1}{4}$  ml tuberculin syringes one for each insecticide and one for acetone control were used. Syringes were rinsed three times in acetone before and after use and between each dosage level. Five pairs of forceps similarly treated were used to handle flies for each solution. Ten adult female flies were treated at each dosage level. A minimum of three complete replicas constituted a test series. Treated flies were transferred to 1 pint wide mouthed Ball type glass jars or to 400-ml glass beakers with double layered, gauze covers. Each container was labeled as to fly strain, insecticide used, dosage, and date treated.

When a colony of flies was of sufficient strength for testing a complete test series was conducted during one day's operation. Flies under test were held for 24 hours at 24 C  $\pm$  2 C after which mortality was recorded for each dosage gradient of toxicant. Our criterion for death was complete cessation of all bodily activity. Tests in which more than one death occurred among control flies were discarded. Knockdowns and loss of muscular coordination were not considered as probable death.

The Thompson method for calculation of the median effective dose ( $M_{50}$ ) was employed in this study. This is the dose of a given agent at which half of the test subjects react critically. The median effective dose like the median is less affected by variation in the extremes of the data than is the LD and therefore is a more stable measure of central tendency.  $M_{50}$  values of 15 to 625 were considered to indicate high resistance, of 5 to 14.9 moderate resistance, of 1 to 4.9 low resistance, and below 1.0 susceptibility.

## RESULTS

As seen in table 1, there was a notable increase in resistance to DDT between 1955-1956 and 1956-1957 in the 11 cases where strains from exactly the same locality could be compared in the two series. To a lesser extent this also was true of resistance to lindane, dieldrin, and malathion, however, in no instance was there more than low resistance to malathion.

*Ryukyu Islands.* Of the six strains tested, high resistance to DDT only was found in four strains, while a fifth strain showed high resistance to both DDT and dieldrin. Moderate resistance to DDT occurred in the one strain from Ishigaki in the 1956-1957 series, whereas in the 1955-1956 series the strain from Ishigaki was susceptible to DDT. Neither high nor moderate resistance to lindane or dieldrin was observed. Low resistance to lindane

TABLE 1 Median effective dose values in micrograms of each of four insecticides exhibited by various strains of houseflies

Source of fly strain	DDT		Lindane		Dieldrin		Malathion	
	1955	1956 1957	1955	1956 1957	1955	1956 1957	1955	1956 1957
Stable A Yokohama	0 41	625 0	1 02	625 0	0 14	625 0	0 02	1 06
Stable B Yokohama	31 0	625 0	5 03	4 64	7 19	625 0	0 04	1 06
Stable C Yokohama	0 36	625 0	3 08	2 19	1 02	625 0	0 01	1 16
Garbage Dump Yokohama	21 47		0 41		0 06		0 05	
Garbage Dump Tokyo	2 70	625 0	0 26	625 0	0 05	625 0	0 01	0 82
Washington Heights Tokyo		625 0		2 12		625 0		0 62
Camp Drake Japan	2 77	625 0	0 53	0 49	0 05	625 0	0 001	1 81
Camp Drew Japan	3 05	625 0	0 36	0 78	0 03	0 21	0 004	1 22
U S Army Supply Center Japan	2 99	625 0	0 16	625 0	0 01	3 77	0 002	0 50
Garbage Dump Sobudaimae Japan		625 0		625 0		625 0		2 26
Johnson Air Base Japan	1 17	625 0	0 49	625 0	0 05	625 0	0 02	1 46
Tachikawa Air Base Japan	1 06	625 0	0 04	0 17	0 003	0 27	0 02	0 56
Fleet Activities (Navy) Yokosuka	5 18	625 0	0 43	625 0	0 001	625 0	0 02	1 40
Awase Okinawa, Ryukyu Islands		625 0		1 17		22 3		0 58
Ishigaki Yaeyama Gunto Ryukyu Islands	0 28	5 74	0 28	0 26	1 63	4 98	0 002	0 46
Ishikawa Okinawa Ryukyu Islands		625 0		0 64		0 99		0 42
Itoman Okinawa Ryukyu Islands		625 0		0 40		3 29		0 59
Kadena Air Base, Okinawa Ryukyu Islands		625 0		0 19		0 33		0 46
Naha Air Base Okinawa Ryukyu Islands		625 0		0 47		0 39		0 20
Seoul Korea	0 23		0 17		0 43		0 02	

only was noted in one strain while two strains exhibited low resistance to dieldrin only. One strain was susceptible to malathion only, two strains to malathion and lindane, and three strains to malathion, lindane, and dieldrin.

*Korea* Tests conducted in the 1955-1956 series showed the strain originating in a garbage dump near Seoul, Korea, to be susceptible to DDT, lindane, dieldrin, and malathion. No strains from Korea were tested in the 1956-1957 study.

*Japan* In the 1955-1956 series 2 of the 11 strains tested showed high resistance to DDT only; none were highly resistant to the other three insecticides. One strain was moderately resistant to DDT only, and two strains to lindane and dieldrin. Six strains had low resistance to DDT only, one strain to lindane only, and one strain to lindane and dieldrin. One strain was susceptible to malathion only, one strain to dieldrin and malathion, one strain to DDT, dieldrin, and malathion, and eight strains to lindane, dieldrin, and malathion.

In the 1956-1957 series high resistance to DDT was demonstrated in all of the 12 strains tested. Two strains exhibited high resistance to DDT only, one strain to DDT and lindane, four strains to DDT and dieldrin, and five strains to DDT, lindane, and dieldrin. No strains exhibited moderate resistance to any of the four insecticides. One strain possessed a low resistance to lindane only, one strain to dieldrin only, two strains to lindane and malathion, and six strains to malathion only. One strain was susceptible to lindane only, one strain to lindane and dieldrin, one strain to lindane, dieldrin, and malathion, and three strains to malathion only.

## DISCUSSION

Peculiarities in strains exhibiting resistance to one or more of the insecticides are of interest. One strain (Stable A, Yokohama) obtained from a cow stable near a U S Armed Forces Dependent housing area in Yokohama, Japan, exhibited high resistance to DDT, lindane, and dieldrin, but low resistance to malathion. Strains Stable B, Yokohama, and Stable C, Yokohama, originating in two similar stables within a one-half mile radius of the former, exhibited high resistance to DDT and dieldrin, and low resistance to lindane and malathion. DDT had been used in these stables over a period of about eight years, while lindane was first used in the summer of 1954 (table 2).

From June through October 1955, each of the three stables received a weekly application of malathion, dieldrin, and lindane on a five-week rotating schedule in a special study to determine the comparative efficacy of those insecticides. Flies collected from these stables following termination of that study were used in tests to determine  $M$  values in the second study series under

TABLE 2 Insecticides used in areas from which test strains of houseflies were obtained

Area	Prior to 1953	1953	1954 <sup>a</sup>	1955	1956
Stable A Yokohama	DDT	DDT	lindane	lindane dieldrin malathion	malathion
Stable B Yokohama	DDT	DDT	lindane	lindane dieldrin malathion	malathion
Stable C Yokohama	DDT	DDT	lindane	lindane dieldrin malathion	malathion
Garbage Dump Yokohama	DDT	DDT	DDT	lindane malathion	
Garbage Dump Tokyo	DDT	DDT	DDT BHC malathion	dieldrin malathion	malathion
Washington Heights Tokyo	DDT	DDT		lindane	
Camp Drake Japan	DDT	DDT		lindane	
Camp Drew Japan	DDT	DDT		lindane	
U S. Army Supply Center Japan	DDT	DDT		lindane	
Garbage Dump Sobudamae Japan	DDT	DDT		lindane	



taken in 1955-1956. New colonies from these stables also were established for the 1956-1957 study.

In tests with the three Yokohama stable colonies for two successive years, flies from Stable A and Stable B increased from susceptible to high resistance for DDT, while those from Stable C maintained their high degree of resistance for that insecticide. High resistance to lindane and dieldrin developed in the Stable A colony. Stable B and Stable C colonies developed a high resistance to dieldrin but maintained a low resistance to lindane. In all three stables an apparent increase in resistance to malathion was noted. In spray operations in these stables during the past 1½ years, 1 per cent malathion has been used at weekly intervals during the fly breeding season.

In the 1955-1956 study, a strain reared from adult flies captured at the Yokohama Garbage Dump was shown to have a high resistance to DDT but was susceptible to lindane, dieldrin, and malathion. Only DDT had been used as the control agent for at least five years, with progressively marked decrease in effectiveness year by year. Malathion spray (1 per cent) applied late in the summer of 1955 quickly reduced the fly population by an estimated 98 per cent. The fly population at the dump has been kept at a low level since that time through the continued use of malathion.<sup>5</sup> Unfortunately,  $M_{50}$  values were not determined for this strain in the present study.

At the Tokyo Garbage Dump, DDT had been used in the control of houseflies for at least five years prior to August 1954, followed by benzene hexachloride (BHC) for a period of three months, after which time a study to determine the comparative efficacy of dieldrin and malathion was undertaken. The ineffectiveness of DDT and BHC was particularly noticeable in 1954. However,  $M_{50}$  values obtained in the 1955-1956 studies indicated only a low degree of resistance to DDT. The strain remained susceptible to lindane, dieldrin, and malathion. In the 1956-1957 study, it was demonstrated that flies from a newly established colony originating in the Tokyo dump had developed a high degree of resistance to the three chlorinated hydrocarbons used in this study, while susceptibility to malathion was maintained. Malathion has been the insecticide of choice since 1955 at the Tokyo dump. Findings of a somewhat similar nature were noted for flies originating from Johnson Air Base, Yokosuka Fleet Activities, and Yokohama Stable A.

Of the 13 strains from Japan and the Ryukyu Islands that were tested against DDT, only one strain, that from Ishigaki City, Ishigaki Island, of the southern Ryukyu Group, had not as yet developed high resistance. However, as the  $M_{50}$  values in the present study indicate, DDT resistance increased appreciably between 1955-1956 and 1956-1957, and the Ishigaki strain may develop high resistance to DDT by 1958.

In general the housefly strains studied have demonstrated progressive development of resistance to DDT lindane dielrin and even malathion one of the newer organic phosphate insecticides Unless control methods against houseflies are modified to an extent whereby the use of the chlorinated hydrocarbon group of insecticides may be discontinued fly strains presently exhibiting moderate or low resistance to these insecticides may be expected to show a continuing increase in resistance within a relatively short time The apparent increase in resistance to malathion exhibited by the majority of the housefly strains tested is of interest and concern but continued observations are necessary before any definite conclusion can be drawn as to the permanency of this phenomenon

### SUMMARY

The median effective dose (M<sub>50</sub>) values for DDT lindane dielrin and malathion were determined for 13 strains of houseflies from Japan 6 strains from the Ryukyu Islands and 1 strain from Korea All strains except one from Ishigaki Ryukyu Islands and one from Korea were highly resistant to DDT and five strains also showed high resistance to lindane and malathion

An appreciable increase in resistance to DDT was noted for 11 strains originating in the same areas and tested in both the 1955-1956 and the 1956-1957 series The same was true of 5 strains tested against lindane, 9 strains against dielrin and 7 strains against malathion A slight decrease in M<sub>50</sub> values was recorded for 4 strains tested against lindane In two such cases strains from Yokohama Stable B and Yokohama Stable C use of lindane spray had been discontinued for about one and one half years Low resistance to malathion was encountered in 8 of the 20 strains tested the remainder being susceptible

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## Clinicopathologic Conference

Madigan Army Hospital Tacoma Wash

### SYMMETRICAL SWELLING OF THE LONG BONES

**Summary of Clinical History** A 9 week old white female infant was hospitalized 9 October because her mother thought the child had a slight cold and noted gurgling sounds in her throat.

The infant was born with clubfeet, absence of both thumbs and both first metatarsal bones. Her birth weight was 7 pounds, 15 ounces. The infant did not gain in weight and several weeks prior to hospitalization she developed "swelling" of the long bones of the extremities. The mother stated that the infant had taken very little nourishment and after taking several swallows would then refuse further feeding. On the day of admission she took only 1 1/2 ounces of formula. There had been some vomiting a week or so after birth. Her stools were normal.

One brother was reported to be normal and in good health. There was no history of familial disease.

**Physical Examination** The patient was an extremely malnourished white female infant with very pale dry skin. Her weight on admission was 6 pounds 13 ounces and her temperature was 98.6°F. The tongue was dry and coated. The ears were large. The throat was not congested. The neck revealed no abnormal findings. The thorax was symmetrical and the breasts were not enlarged. The lungs were resonant, harsh breath sounds were heard over the anterior chest suggestive of a pleural friction rub. No areas of dullness were heard posteriorly and the breath sounds were audible. No rales were heard. Auscultation of the heart revealed no murmurs. The abdomen revealed no tenderness, distention or palpable masses. Examination of the back and genitalia revealed no abnormal findings. Both

Brig G J ck W Schw rtz MC USA C mma ding Ge tal Fr m th Labor t ry  
S rvic Lt C l William C. Butz MC USA Chief



thumbs were absent toes 1 and 5 of both feet were much shorter than the other toes The long bones of the arms and legs and the bones of the skull were described as thickened

**Laboratory Studies** Red blood cells numbered 2 000 000 and the white blood cells 30 000 per  $\mu$ l with 2 per cent eosinophils 1 per cent metamyelocytes, 13 per cent band forms 65 per cent neutrophils 1 per cent monocytes and 18 per cent lymphocytes The hemoglobin was 7 grams per 100 ml

**Course in Hospital** On admission the infant was dehydrated anemic and taking feedings very poorly On 11 October a whole blood transfusion of 75 ml was given intravenously In addition the child received crystalline penicillin and Ringer's lactate glucose solution by hypodermoclysis Gavage was taken very poorly and was followed with the production of excessive mucus and some difficulty in respiration There appeared to be resistance to the gavage tube at about the 5 cm level suggesting the possibility of a tracheoesophageal fistula The daily intake of fluid ranged from 170 to 550 ml The temperature curve was irregular with daily elevations reaching  $102.6^{\circ}\text{F}$  on 15 October The patient's course progressively worsened, with increasing pulmonary insufficiency On 16 October the infant died with a temperature of  $103^{\circ}\text{F}$

## DISCUSSION

**D + H** I believe that the immediate cause of death in this case was the respiratory infection more specifically an aspiration pneumonia My primary diagnosis is a type IV + H type tracheoesophageal fistula I shall consider the case from three angles first the symptoms attributable to a congenital defect of the esophagus second from the standpoint of the anemia and third from the standpoint of the skeletal findings

Certain symptoms attributable to an esophageal defect are provided These include (1) excessive mucus following feedings (2) the statement that the baby would take several swallows and then refuse further feedings and (3) the physical finding of a malnourished baby The case is also mentioned in connection with the passage of the gavage tube

A consideration of the causes and types of esophageal lesions is in order First the tracheoesophageal fistulas will be discussed The incidence of tracheoesophageal fistula varies from 1 in 500 births in Boston to 1 in 10 000 births in Philadelphia Ninety seven per cent of the cases of tracheoesophageal fistulas are associated with atresia There are four types of tracheoesophageal fistulas The most common type is the condition in which an upper segment of esophagus ends in a blind pouch at about the level of the bifurcation of the trachea or slightly above and a lower segment from the stomach is connected

to the trachea by a short fistulous tract. Much less common is the state in which both upper and lower esophageal segments are blind, neither being connected to air passages. The third type is one in which the upper esophageal segment opens into the trachea and the lower segment is a blind pouch. The rarest type (type IV) accounting for from 1 to 10 per cent and usually reported in about 3 per cent of the cases is a communication between the intact esophagus and the trachea or bronchus through a small fistulous tract that may be very difficult to demonstrate.

This fourth type is the variety that this patient most likely would have because if the child had any others with an atresia, death would have occurred sooner. The symptoms of this fourth type of tracheoesophageal fistula, the H type, usually include coughing, choking, and cyanosis with the first few feedings. History of these symptoms is not provided; however, there is no denial of that fact in the protocol. The baby usually takes to the nipple early and takes a few swallows and then chokes and may become cyanotic and refuse further feeding so that the infant in time usually becomes malnourished.

In 1955 there was reported from St. Louis a series of three cases.<sup>2</sup> The patients' ages were 1 month, 6 weeks, and 23 days. Autopsy was performed on two of these; the third received surgical correction and was apparently well following the surgery. However, this does prove that with this fourth type of tracheoesophageal fistula infants can live to this age. In fact, the first patient who was successfully operated on was 6 years old. In 1939 Imperatori<sup>3</sup> described a case of a 6-year-old child in whom pyloric stenosis was suspected and the baby was operated on without benefit. Throughout infancy and early childhood therapy continued to be directed toward dilatation of the cardia by administration of antispasmodics, sedation, and use of mechanical dilators. Chronic pulmonary disease retarded physical development and general poor health persisted until the presence of a tracheoesophageal fistula was demonstrated in the sixth year of life. Imperatori then operated on the baby and found a fistula 13 cm long between the trachea and esophagus. A plastic closure of the fistula was performed and a permanent cure was obtained with the return of good health.

Concerning the diagnosis of this type of fistula, it must be recognized that the tract may be so small or its course so devious as to impede the passage of contrast media such as Lipiodol. Under certain circumstances an aqueous contrast medium such as a 35 per cent solution of Diodrast is indicated. The treatment indicated is surgical and if the baby dies, which is not uncommon, the cause of death is an aspiration pneumonia. Another possible anomaly consists of a short esophagus. In such a case a portion of the stomach is displaced upward through the diaphragm into the thoracic cavity. The stricture is at the cardia in the midthorax with the short esophagus above it and the free gastric mucosa below it. The rugae can be followed through the diaphragm as a continuation of the rugae of the subdiaphragmatic stomach. The fact

that the card becomes stenotic accounts for the symptoms. The clinical picture is characterized by dysphagia, regurgitation, malnutrition, and frequent attacks of complete obstruction of the esophagus. When there is stricture the only treatment is repeated dilatations which are often unsuccessful and one must resort to gastrostomy. Death in childhood is unusual and if it occurs it usually results from an aspiration pneumonia.

Another possible lesion might be a congenital stenosis of the esophagus either as a web or as a segmental narrowing of the lumen. This lesion would cause symptoms similar to those of the congenitally short esophagus. However, the symptoms are less severe, less often fatal, and respond more readily to esophageal dilatation than the congenital short esophagus. Another possible lesion could be a congenital vascular ring encircling the trachea and esophagus. In this instance, however, the patient would have symptoms of a croupy cough and laryngeal stridor as well as symptoms of esophageal compression. The most common type of congenital vascular ring is a persistence of both arches of the aorta with one arch being larger than the other. The ring thus formed encircles the trachea and esophagus. This would cause no disturbances in circulation but would cause definite symptoms of difficulty in swallowing and breathing. However, there should be a croupy cough and laryngeal stridor which are not recorded in this case. Other anomalies of the large vessels may also produce these vascular rings. A right aortic arch may occur in combination with a left descending aorta. A right aortic arch may be associated with a left subclavian artery arising from the dorsal root of the aorta compressing the trachea and esophagus. A compression of the esophagus and trachea could be produced by an aberrant right subclavian artery which arises as the last branch of the arch of the aorta. However, any of the esophageal rings would produce symptoms of a croupy cough and laryngeal stridor.

In addition to the primary diagnosis the skeletal findings are regarded as associated lesions. Some of the possible diagnoses will be discussed. The diagnosis of chondrodystrophy is usually readily made by inspection. The characteristic skeletal features may be present at birth, however, these manifestations may be incomplete or somewhat atypical. In the latter event roentgenographic examination of the long bones will be of a most helpful help. The clinical features result from the retardation of endochondral osteogenesis including the epiphyses while periosteal bone formation continues in a normal fashion. The extremities, especially the thighs and upper arms, are characterized by markedly shortening and increased width. The normal curvature are exaggerated. The hands often may not extend much below the waist. Enlargement of the epiphyses may limit extension of the shoulders. The head is relatively large and the forehead and mandible prominent. The bridge of the nose is depressed while the tip is broad and turned up. The medial portion of the clavicle grows normally because of its membranous origin while the lateral portion

which is endochondral in origin demonstrates impaired growth. This may cause outward and upward buckling of the clavicle. The length of the vertebral column is relatively normal and is the important part in differentiation from Morquio's disease (chondroostodystrophy). Lordosis, protrusion of the abdomen and prominent buttocks are other characteristic features. The stature is of course lower than normal.

Osteopetrosis or Albers-Schönberg disease is a rare disorder characterized by the hardness and brittleness of the bones. The patient often has a hypochromic anemia and in the final stage of the disease a myelophthisic anemia. The roentgenographic appearance of the bones is diagnostic. The cortex of the bones as well as the trabeculae are thickened. The increased density of the entire skeleton is the essential feature. No distinction can be made between the cortex and the marrow. There are heavy shadows at the base of the skull and the bones of the cranial vault appear less dense.

Caffey and Silverman<sup>4</sup> described the condition of infantile cortical hyperostosis in which hyperostosis has been observed in the calvarium, mandible, clavicles, scapulas, ribs, and the long bones of the extremities, including the metatarsals. The clinical features vary to a considerable degree but as a rule the symptoms are not severe. Fever is usually of low degree. Tenderness, irritability, pseudoparalysis, dysphagia, pleurisy, increased sedimentation rate, and elevated serum phosphatase have been observed in several combinations. The occurrence of the syndrome is limited to the first six months of life. Recovery has occurred in all recorded instances with no residual defects, so it would have to be an incidental diagnosis in this case. A similar clinical picture may occur in infants with vitamin A poisoning. However, the symptoms do not occur until the latter half of the first year of life, and there is no facial or mandibular swelling as in infantile cortical hyperostosis. Caffey<sup>5</sup> also stated that he had never seen a case of scurvy in the first three months of life. Likewise this case is probably too young for rickets. Osteochondritis due to congenital syphilis may occur during the first three months of life. However, in congenital syphilis the liver is almost always enlarged and there is usually some degree of jaundice as well as an enlarged spleen and lymph nodes, mucocutaneous lesions, and skin lesions, all of which are not present in this case.

Now to consider the patient's anemia. I consider it to represent an anemia of infection. Congenital leukemia is rare but has to be considered. However, the lymph nodes, spleen, liver, and kidneys are usually enlarged. The hematologic tendency is almost universally present and is manifested by petechial purpura and extensive ecchymosis. In 1927 Franco<sup>6</sup> reported the course of an infantile anemia in association with multiple congenital anomalies. In three cases of this type. These children had hypoplasia of the heart, hypoplasia of the lungs, exaggerated tendon reflexes, and congenital anomalies of the skeleton. In all three cases there have been no attacks of the heart and lungs.

urinary tract and most consistently defects of the bones of the arms and hands. Cleft palate has also been noted. Attention is usually first called to these patients by the presence of anomalies at birth.

The anemia becomes manifest in a few weeks. It is progressive and unrelieved except by transfusion. Ecchymoses and hemorrhage from the mucosal surfaces may occur early and usually recur often. Cranulocytopenia renders these children susceptible to frequent and severe intercurrent infection. The treatment is limited to the liberal use of antibiotic drugs and transfusions of whole blood. Few patients survive the early years of childhood. However in this case anemia is not an aplastic type and there are no hemorrhagic tendencies. No evidence whatsoever exists that this anemia is due to a hemolytic mechanism. So again I feel that the cause of death is aspiration pneumonia and the primary diagnosis is a type IV or H type tracheoesophageal fistula.

**D r B r :** Have you explained the bone lesions and can the entire clinical picture be brought together?

**D r H :** No I haven't. I have to consider the bone lesions as associated findings. I mentioned the diagnoses that include the bone lesions. I tried to think of processes where the diagnosis would explain the whole entity and cannot find any disease that would suffice. Therefore I thought that this was probably more likely a type IV tracheoesophageal fistula with the bone findings as an associated condition. One condition I considered was that the bone lesions could be associated with scurvy. Of course Caffey stated that scurvy does not occur this early. This is true if you think of malnutrition as being responsible for scurvy. The protocol does not mention painful extremities which they should be if they were swollen as the result of a subperiosteal hemorrhage.

In talking about these bone lesions one has to think of several more entities. First of all this is not osteopetrosis or Albers-Schonberg disease which reveals a white uniform type of sclerosis of all the bones. It originally occurred to me that there are relatively normal looking bone outlines that outside the cortex there is calcification and I presume new bone formation in all the long bones. One must think of trauma here. It is possible that a youngster subjected to head blows or rough handling of the extremities could have such a type of lesions although most of the time he would also have fractures but the physical picture is one of subperiosteal hemorrhage and new bone formation in all the bone. I cannot see how this youngster could have such trauma in all extremities.

I think that we do have to try to tie this up into one disease or entity that produce the anemia and the bone changes besides the congenital malformations of the fingers and toes. The disease that I think would do all this would be Fanconi's hereditary congenital anemia. I wish that it were complete anemia such as a pancytopenia.

rather than a normocytic anemia. This child did have a good elevation of the white count but to account for all these three features I must diagnose the disease as Fanconi's anemia.

Doctor Schwartz: Doctor Maki, will you discuss the x-ray findings please?

Doctor Maki: A single anteroposterior view of the skeleton demonstrates that there is marked thickening of the periosteum of the long bones (fig 1). I think the scapulae also are involved. This appears to be the most significant abnormality. I think that Doctor Harris brought up a very good point in saying that this thickening may be due



Figure 1 Roentgenogram of patient showing extensive deposits of subperiosteal new bone on long bones of extremities.

to trauma. In the time I have been here I have seen two cases of trauma in which there was marked periosteal thickening of the extremities on both sides but not the degree of extensive and progressive involvement present here. A differential point in Fanconi's disease in which there

is extensive kidney damage as well as the presence of osteoporosis. Some of the other diseases to consider of course would be scurvy and rickets both of which would also demonstrate osteoporosis. In rickets the changes are predominantly in the growth cells at the ends of the bones and here especially at the distal ends of the tibia a fair state of normal ossification is apparent. There isn't any osteoporosis, saucerization, widening or any of the other features which are present in rickets and the same holds true for scurvy. With scurvy there would be more ballooning of the periosteum. In this case the changes are symmetrical on both sides.

Infection perhaps should be considered but can be excluded almost immediately. It is most unusual to have such extensive involvement resulting from either tuberculosis or osteomyelitis. Certainly if there was involvement in only one bone infection should be considered. With tuberculosis the changes are mostly those of destruction which may be localized. In the latter instance the only location in which there is thickening of the bone or periosteum is in the metacarpals and phalanges or the metatarsals.

Osteopetrosis or marble bone can be excluded because in this condition there is a homogeneous appearance of the bone whereas in this case the cortex and the marrow are actually visible beneath the periosteal thickening. This is not true with marble bone disease. Von Eschmann disease is another condition to consider but this is usually discovered at a later date, at about 8, 9 or 10 years of age and again there is symmetrical thickening of the diaphyses. In addition the nutrient foramina are enlarged and pronounced.

Hypervitaminosis A as Doctor Harris has mentioned is not likely because it is not usually seen before the age of one and in that condition there isn't as much generalized thickening and it is usually more symmetrical.

Caffey's disease probably explains all the findings in view of the fact that in Caffey's disease there is involvement of the scapulas, symmetrical periosteal thickening of the long bones and the mandible is involved in almost all cases. The age group is right. Last spring (1955) Doctor Caffey was in Seattle, Wash. and presented a paper on this disease. In a number of cases he was actually able to make the diagnosis in utero when the patients presented themselves for pelvimetry studies. I think the findings here probably would fit those of Caffey's disease.

A Phy: Can you rule out syphilis?

Dr. Mak: In congenital syphilis the changes are found in the ends of the long bones. The tibias may show periosteal thickening and ossous destruction may be present in the proximal ends. This is called Wimberly sign.

A Phy: Doctor Mak, does not this sign appear a little late in life? This is a young child.

Doctor Maki: This is true with respect to the thickening of the tibia. That is a later sign but other signs are found early. Periosteal thickening is usually confined to the tibia on the convex side.

A Physician: What is Caffey's disease?

Doctor Maki: Nobody knows. The other name is infantile hyperostosis corticalis. It is of unknown etiology and as Doctor Harris mentioned it is a self-limiting disease. Patients become perfectly normal after 6 months or a year of life.

Doctor Pophal: Any other comments?

Doctor Tomsovic: This baby was born with multiple congenital anomalies. The child had difficulty in swallowing and maintaining its nutrition from the time it was born which suggests the existence of yet another congenital anomaly. To go back a step further, the cause of the congenital anomalies may have been something which occurred during the course of the pregnancy. There may have been a nutritional injury to the fetus. If the mother's nutrition is poor, the baby may be born with congenital anomalies and may begin life with a poor nutritional endowment. If the mother had a poor diet, the infant might have had to start life with a relatively poor store of iron (this may have had bearing on the anemia). Likewise, the child might have had a relatively low store of vitamin C which coupled with a deficit present at birth could lead to clinical scurvy before the usual age of onset. The periostitis requires a separate explanation since it does not fit the rest of the picture of multiple congenital anomalies.

Now let us consider Fanconi's syndrome. There are two syndromes bearing Fanconi's name. One is a metabolic error producing aminoaciduria, glycosuria and the kidney changes which have been described. The second Fanconi syndrome is the one referred to in this case. This is characterized by congenital anomalies in the hands and forearms, particularly absent thumbs, pigmentation involving genitalia and axillae and a severe anemia which is quite refractory to treatment. This I believe is the principal diagnosis.

I do not believe that the story is consistent with tracheoesophageal fistula. There are types of tracheoesophageal fistulas that produce trouble immediately after the baby is born and there are types in which the infants progress satisfactorily for a period of time. Almost all of the latter which appear by 2 months of age show evidence of pulmonary aspiration. The esophageal obstruction seems to me therefore to be due to some other type of abnormality, most likely a vascular ring.

I would diagnose this as a case of Fanconi's syndrome with congenital hypoplastic anemia with an obstructive lesion of the esophagus.

Capt. Wahl, J. Pophal, MC USA, Assistant Chief Laboratory Section

Maj. Edward R. T. Miller, MC USA, Chief Pathologist, Service Department

M.D.



agus most likely a vascular ring with scurvy secondary to nutritional deprivation

**A Phy** How can one differentiate between the two types of Fanconi's syndrome?

**D r T m l** I think it would be hard to make a diagnosis of Fanconi's syndrome the type with anemia in an infant of 9 weeks. It is only after following the patient with repeated blood counts and demonstrating a consistently low hemoglobin without other apparent cause that the diagnosis usually becomes evident. I think it would be almost impossible to make a diagnosis of Fanconi's syndrome with certainty in such a young infant. The other Fanconi's syndrome so-called de Toni-Fanconi syndrome is excluded clinically by negative urinary findings.

#### **Doctor Harris Diagnoses**

- 1 Tracheoesophageal fistula type IV
- 2 Fanconi's syndrome
- 3 Pneumonitis bilateral aspiration type

#### **Doctor Tomsovic's Diagnoses**

- 1 Fanconi's syndrome with congenital hypoplastic anemia
- 2 Esophageal obstruction due to a vascular ring
- 3 Scurvy secondary to nutritional deprivation

#### **Doctor Maki's Diagnosis**

- 1 Infantile cortical hyperostosis (Caffey's Disease)

### **PATHOLOGIC FINDINGS**

**D r P ph l** This is a case of Caffey's disease. The immediate cause of death was severe bilateral bronchopneumonia. A tracheoesophageal fistula was not present; however, there was distal narrowing in the first portion of the esophagus and although it was not mentioned in the history, I feel that aspiration due to the stricture may have played some part in bringing about a pneumonitis in this child. The anemia was probably secondary to inadequate nutrition resulting from this stricture and also due to infection. The anomalies of the hands and feet (arthrogryposis multiplex congenita) were incidental to the death of this infant because it has been stated most of these infants recover spontaneously.

Most cases of Caffey's disease occur before the age of 4 months although there is at least one case that began at 20 months. There is no sex preference. Most patients are Caucasians although one reported was a Negro and one a Chinese. The family history is not contributory. In at least one instance there was reported more than one case in a family but not at the same time. Most cases first become manifest with irritability usually associated with fever and sometime the febrile swelling develops, most often noted in the long bones. In a short time bone deposits are laid down in the areas of swelling. Some of these deposits are so small that they cannot be

palpated and in other areas the enlargement and bone formation is so extensive as to produce a gross enlargement. The swellings have been reported in all parts of the skeleton except the phalanges, small bones of the carpus and tarsus, vertebrae and pelvis. Associated findings include anemia, leukocytosis, elevated sedimentation rate, fever, and pleurisy. In some cases it was believed that the pleurisy was associated with changes in the ribs adjacent to the pleura, but pleurisy has also occurred in cases without involvement of adjacent ribs, so it is not a constant feature. The skeletal pathology involves a severe thickening of the periosteum with a gelatinous character and dense fibrous bands extending from the periosteum into the adjoining tissue. Some observers have stated that these fibrous bands even extend to the skin. The periosteum is edematous and vascular, but there is no inflammatory infiltration or hemorrhage. Then there is extensive formation of subperiosteal bone which is unorganized and is extremely vascular. The marrow spaces are fibrous. The cells of the marrow have been described as lymphocytoid cells or cells resembling micromyeloblasts. This disease is characterized by exacerbations and remissions, and with these exacerbations and remissions additional layers of cortical bone are laid down. The muscles adjacent to the bone show degenerative changes and the arteries reveal intimal proliferation, such that some observers have wondered if this disease begins in the soft tissues rather than in the bone. The original cortex is well preserved for a time but as the process progresses, thinning of the cortex is observed, there being a widening of the medullary cavity with regression and osteoporosis, but eventually the bone returns to normal.<sup>7</sup>

The typical appearance of these infants, described as a moon face, is the result of thickening of the bones of the skull, particularly the mandible. The original cortex is relatively undisturbed. This section through the knee joint reveals that the cortical hyperostosis does not extend beyond the epiphyseal line (fig. 2). Some of these children have distinct limitation of motion of the joints and in this patient there were adhesions between the synovia and joint surface.

The periosteum is edematous, greatly thickened, and cellular. There is no leukocytic infiltration or hemorrhage to indicate an inflammatory process (fig. 3).

A higher magnification of the subperiosteal new bone shows extensive osteoblastic activity, and yet there are a surprising number of osteoclasts in some areas. No Haversian systems are noted. The bone is unorganized. The marrow substance is cellular, slightly fibrotic and very vascular (fig. 4).

In a section taken at the epiphyseal junction (fig. 5) there is disorderly growth and the epiphysis is wide. The etiology of this condition is unknown. Many factors have been considered—*infection, allergy, excess of vitamin A, et cetera*—and many tests have been made. These lesions have been cultured, not only for bacteria but also for viruses.



Fig 2 Section of distal end of femur showing grossly sclerotic bone formation. The osteomyelitic body is physeal.



Figure 3 Photomicrograph of periosteum showing marked cellular thickening but absence of hemorrhagic activity.

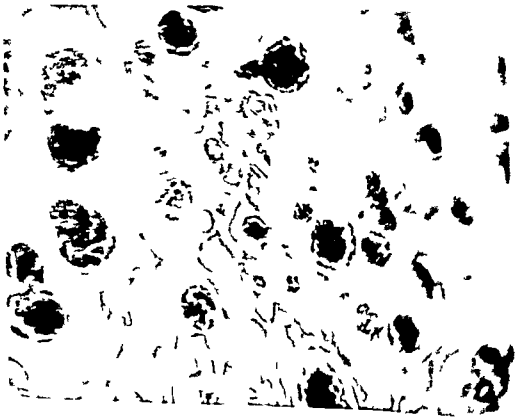


Figure 4. Photomicrograph of new immature bone. The trabeculae and the marrow spaces contain vascular filigree.

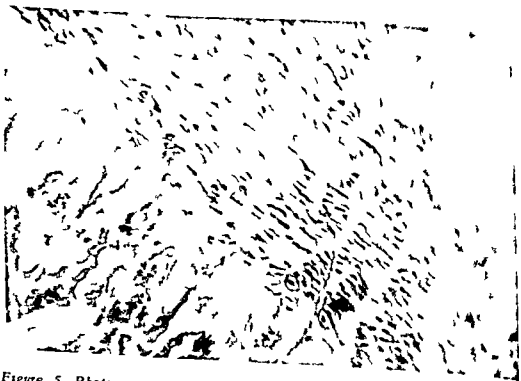


Figure 5. Photomicrograph of epiphysis revealing disordered growth of columns.

and they have been negative Tests for typhoid paratyphoid brucellosis and various other conditions have been negative Various types of treatment have been tried but to date none have been helpful Most cases recover spontaneously

### Pathologic Diagnoses

- 1 Bronchopneumonia bilateral
- 2 Congenital esophageal stenosis first portion
- 3 Infantile cortical hyperostosis (Caffey's disease)
- 4 Arthrogryposis multiplex congenita

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## THE CHANGING PATIENT

Medicine is still a private art. The physician's confidential patient approach is the same as ever. The change is mainly in the patient. He may not have the faintest idea of the functional relationships within his glandular system but at least he is aware and can cooperate with the physician in his treatment. Even if he doesn't understand the *Reader's Digest* article he has an interest which must be put to good use. To him or her medical news may only be an abstraction or gossip but the physician—and the physician alone—has an opportunity to convert it into a promise or hope come true.

—HENRY S. M. NEIL

*J. m. l. f. S. th. C. l. M. d. l. A. ci. t.*  
p. 260 J. ly. 1957

## SERVICE ARTICLES

# NUTRITION SURVEYS IN THE NEAR AND FAR EAST

Report of the Interdepartmental Committee  
on Nutrition for National Defense

FRANK B. BERRY *M.D.*  
ARNOLD E. SCHAEFER *Ph.D.*

THE enthusiastic and continued interest in nutrition improvement shown by the six countries in the Near and Far East where the Interdepartmental Committee on Nutrition for National Defense (ICNND) has conducted surveys during the past two years is evidence that this form of technical assistance is well accepted. During our visits to the Near East in the fall of 1956 and 1957 people repeatedly expressed thanks—and sometimes surprise—that the United States is interested in the welfare of men in other nations—in their health and their food. In most of the developing countries visited, the primary concern of the majority of the people is survival, which is dependent on food and shelter. These seem far more important to them than the possibility of war and destruction.

The work of the nutrition teams is carried out on a partnership basis with scientists and technicians of the host country working with the United States members. The latter have reported that the nutrition studies are an effective form of scientific-military aid which often can be expanded and applied for improving the health of the civilians. The success of this type of mutual assistance is due in large part to the understanding, co-operation, and wholehearted support received from host country governments and military groups, U. S. Government agencies, and Military and Economic Assistance Missions.

Much credit is due our armed services, the U. S. Public Health Service, and the many universities and colleges that have released key personnel for the survey teams. The following educational institutions have participated: Vanderbilt, Cornell, Illinois, Maryland, Harvard, Rochester, Tulane, Temple, Agricultural and Mechanical College of Texas, Oregon State, Pennsylvania State,

and Virginia Polytechnic Institute. The U S Army Medical Nutrition Laboratory, the National Institutes of Health, and the Office of the Surgeon General of the Army also have supplied personnel, while laboratory support has been obtained from the Naval Medical Research Unit No. 3 in Egypt and the 406th Medical General Laboratory in Japan.

We all are familiar with the role that food, nutrition, and health play both in a military operation and in daily life. The old saying that "An Army marches on its stomach" has not changed today. We may have atomic power to propel ships and generate electric power, but no such concentrated substitute for supplying man with energy has been developed. Calories for human propulsion and warmth are still derived from fats, proteins, and carbohydrate. Fuel and hardware are logistic problems, but food is a problem both of logistics and of health.

Sufficient data have been accumulated to state unequivocally that military equipment aid is a poor investment unless the personnel are physically capable of utilizing it with maximum effectiveness. This is not possible when the performance of some 50 per cent of the personnel is impaired by nutritional deficiencies when training hours must be curtailed due to physical exhaustion and when lack of a field type ration reduces effective mobility regardless of the degree of mechanization of the armed forces.

During the past few years our Government has recognized the importance of food and nutrition as an integral part of the Mutual Defense Assistance Program of technical, military, and economic aid. At the close of World War II, the nutritionists of the United States and its allies were called upon to assist in Europe in diagnosing and recommending measures to alleviate problems of acute starvation associated with a secondary protein deficiency.

In Asia and Africa the nutritional problems are much more complex and their solution more difficult. To begin with, in sharp contrast to the large background of data available on Europeans, there is little factual information available on the nutritional conditions and requirements, food production, habits, customs, and taboos of many Asiatic populations. The countries included in the present program are keenly aware of the seriousness of their feeding and nutritional problems and have indicated a desire for assistance.

#### FORMATION AND FUNCTIONS OF THE ICNND

The Committee was organized as the result of a study of the Korean Army and of our efforts to assist the Chinese Nationalists on Taiwan in 1953-1954. One of the findings was that much of the data in reference to food and nutrition which had been collected previously was not generally available to the groups having operational responsibilities in this area. No less than six

different groups were independently making studies in Taiwan. A co-ordination of these studies was indicated to effect economy and to consolidate the recommendations.

In July 1954 an ad hoc co-ordinating committee on nutrition problems was organized at the National Institutes of Health, Bethesda, Md., under the sponsorship of the Department of Defense, with representatives of the departments and agencies with interest in and operating responsibilities for the Mutual Defense Assistance Program. The ICAND was formally established early in 1955 by a memorandum of agreement signed by the Secretaries and heads of departments of interested agencies (Departments of Defense—Army, Navy, Air Force—State, Health, Education and Welfare, and Agriculture plus the International Cooperation Administration). It was later expanded to include the Atomic Energy Commission. Membership includes representatives from the above agencies.

The Committee has a Secretariat consisting of an Executive Director, a nutritionist, a clinician, and an agricultural economist, with offices at the National Institutes of Health. The late Dr. Harold R. Sandstead served as the first Executive Director until his untimely death in November 1955. A panel of 20 consultants who are specialists in the fields of nutrition, medicine, biochemistry, food technology, and agriculture serves as an advisory body, and four subcommittees of consultants have been appointed to consider standard methods for nutrition surveys, nutritional requirements and working standards, nutrition research programs for foreign countries, and food and agriculture.

The purpose of the Committee is to deal with nutrition problems of technical, military, and economic importance in foreign countries in which the United States has a special interest. The Committee serves as a central clearing house on food and nutrition information, evaluates problems of food procurement and feeding, prepares reports and recommendations for the agencies concerned, reviews nutrition projects being conducted in areas where the United States is giving assistance, and co-ordinates, advises, and participates in field projects, when appropriate.

#### NUTRITION SURVEY PROGRAM

In April 1955 and in November 1956, representatives of the ICAND visited a number of countries in Asia and Africa. Following these visits the Committee received requests from the governments of Iran, Pakistan, the Philippines, Turkey, Korea, and Libya for nutrition surveys of their armed forces. The first surveys were begun in January 1956 in Iran and Pakistan, and surveys now have been completed in all six countries. Funding was arranged through the Assistant Secretary of Defense for International Security Affairs as part of the Mutual Defense Assistance



Program the cost to the United States averaging only about \$53 000 per country surveyed

**Objectives** The objectives of the nutrition surveys can best be summarized by three words *assess assist and learn* The assessment phase involves an evaluation of the nutritional status of the population and the capabilities and potential for improving the health of the people In conjunction with the surveys immediate assistance is given as follows (1) by training host country personnel in nutrition evaluation techniques emphasizing clinical and biochemical phases and dietary intake and food production studies (2) by furnishing essential laboratory equipment and supplies for establishing a permanent medical nutrition and food laboratory and (3) by defining the major nutrition problems and developing practical recommendations so that the host country can best utilize the resources within the country

The surveys afford an excellent opportunity for United States personnel to learn much from these countries regarding nutritional diseases foods and food habits and customs and practices Also the clinical biochemical and dietary data obtained contribute to a better understanding of nutritional diseases

**Implementation** Upon request for assistance from a country under the Mutual Defense Assistance Program the ICNND organizes a nutrition team by appointing specialists in the fields of medicine nutrition food technology agriculture and sanitation For most surveys the United States nutrition team members include a survey director one or two clinicians three biochemists two food and dietary survey specialists (usually former U S Army nutrition officers) a food technologist and agricultural economist and a sanitary engineer The host country furnishes counterpart personnel laboratory space and other logistical support About 70 to 90 days are required to make a survey

**Procedures** A *Manual for Nutrition Surveys* has been prepared to serve as a detailed guide for conducting surveys and a revised edition incorporating the experiences of the first four field studies is in press at the U S Government Printing Office The primary purposes of the *Manual* are (1) to establish uniformity in methods techniques and procedures so that a reliable comparison may be made of results of surveys within and among countries (2) to serve as a reference to ensure maximum coverage of the major facts considered essential in appraising nutritional status to permit practical effective recommendations and (3) to define the responsibilities and duties of various team members

The clinical team conducts a physical examination on a statistical sample the number being determined by the population size In general about 2 000 persons are given a detailed examination and an additional 3 000 to 5 000 are given abbreviated physical

examinations that are limited to selected major signs of nutritional significance

Samples of urine and blood are obtained from about 500 of the subjects receiving a complete physical. The biochemical analyses include determination of hemoglobin, hematocrit, plasma protein, vitamin C, carotene, and vitamin A, and urinary excretion of thiamine, riboflavin, and N<sup>1</sup> methyl nicotinamide. The biochemical team is equipped to determine total serum cholesterol and serum albumin and globulin, and to conduct vitamin saturation tests if findings so dictate.

The food and dietary team determines daily food intake by inventory and food preparation survey techniques, and collects composite food samples for chemical analysis. In addition, data are collected on food issues, menu planning, and food habits. The agricultural economist and food technologist surveys food production, preparation, processing, storage, and transportation.

### HIGHLIGHTS OF SURVEY FINDINGS

**General Observations.** Although there are many similarities in the food and nutrition problems in the countries surveyed, each country must be considered separately and practical recommendations made for the solution of individual problems. Two factors affecting the nutritional status of developing countries are lack of adequate transportation to move food from the area of origin to other parts of the country where these foods are in short supply; and lack of processed foods, resulting in considerable quantitative and qualitative fluctuation of food intake during different parts of the year. This lack of processed foods also curtails efforts to develop a field type ration.

Cooking facilities in most of the kitchens consist primarily of large round bottomed pots, either iron or tinned copper, often mounted over a dried clay firebox. Most kitchens prepare food for battalion size units, and the meals are of the one pot type, which is a stew or a soup. This is supplemented with bread in the wheat-eating countries, or a side dish of rice in the rice-eating areas. Typical kitchens are shown in figures 1-3.

Other kitchen equipment usually is very meager, consisting primarily of stirring equipment, pails, knives, and a miscellaneous collection of containers. In most cases there are no mess halls, and each unit brings a large container to the kitchen where a measured amount of the food, depending upon troop strength, is issued. This is taken to the barracks, where the individual issue is made.

As one would expect, cooking facilities are less adequate with smaller units at outlying posts. In general, it is in these units that nutrition problems are most exaggerated. Most foods

are procured from local contractors and in many cases fresh vegetables are purchased by individual units. Since refrigeration and preserved foods are extremely limited virtually all perishables are issued on a 24 hour basis.



Figure 1 Typical pit system for cooking and laundry in a field kitchen.



Figure 2 A military field kitchen. The tent is built on a wooden platform.



*Figure 3 More permanent type of Korean military field kitchen with walls and thatched roof*

Improvement of health and sanitary conditions is dependent largely upon active participation and direction by the Command. In nearly all armed forces, this authority has been delegated. However, preventive medicine, which includes sanitation, housing, feeding, and disease control, is of necessity a Command function.

In most of the countries there is need for improvement in the basic ration allowance and in menu planning, with consideration given to the nutritional adequacy as well as to the cost of a ration.

In general, the principal nutritional deficiencies encountered in the countries surveyed were of riboflavin, thiamine, vitamin A, and vitamin C. Not every country has problems involving all of these vitamins, and in most cases, not all the areas within a country have such problems. Suboptimal intakes of these essential nutrients can, when sufficiently aggravated, result in serious physical disability of the troops. A man with scurvy, beriberi, or night blindness becomes a hospital patient and not an effective soldier.

**General Recommendations** The teams recommend that a nutrition service be established, with representation from the medical, veterinary, and quartermaster departments, and that this group establish close working relationships with civilian experts in the fields of nutrition, agriculture, food technology, transportation, and storage. Some of the principal duties of this service would be to assist Command in (1) formulating basic ration allowances



In both the Philippines and Libya, it was surprising in view of the dietary intake data that the incidence of clinical indicator lesions of riboflavinosis was very low. In reviewing the data, however, other factors must be considered, for in both countries the dietary intake of thiamine was about 30 to 50 per cent of that in the other four countries surveyed. If data from experimental animals can be applied to man, the observed urinary excretion of riboflavin may have been disproportionately high, inasmuch as it has been shown that chronic thiamine deficiency in rats tends to increase excretion of riboflavin. Regardless of the physiologic result or adaptation, the riboflavin intake must be considered deficient according to present-day knowledge.

*Thiamine* Two of the countries surveyed (Korea and the Philippines) are primarily rice eating populations. The observations shown in table 1 indicate a marked difference in the thiamine nutriture of the population groups studied in these two countries.

In the Philippines highly polished rice, which greatly lowers the dietary thiamine intake is used. Although there is provision for rice enrichment in the Philippines, only a small part of the rice purchased by the armed forces is enriched. In one area where enriched rice was used the average dietary intake of thiamine was about 0.3 mg greater than in areas where unenriched rice was used, and the percentage of troops excreting low levels of thiamine was greatly reduced (from 29.5 per cent to 7.9 per cent). In Korea, the armed forces use only undermilled government rice, with a thiamine content of about 0.25 mg per 100 grams. However, most rice for civilian consumption is polished, with a thiamine content of only 0.18 mg per 100 grams.

*Vitamin C* In general, the vitamin C status of the personnel examined varied greatly within the countries surveyed. In one area of Turkey 40 per cent of the troops had blood serum vitamin C levels of less than 0.1 mg, in another area, only 2 per cent of the troops had correspondingly low levels. In four of the countries a large percentage of those examined had low levels of serum vitamin C and dietary intakes were as low as 15 mg per man per day although no cases of overt scurvy were noted. In some areas however, the high incidence of scorbutic type gums left little doubt that lack of vitamin C is a serious problem.

*Vitamin A* There was a great variation in vitamin A intake within each country. In Iran the average intake was about 3,700 I U but with a range of from 400 to 5,000 I U per man per day. It is realized that dietary intake figures based on a relatively short period do not truly represent the vitamin A nutritional status of the individual, because vitamin A can be stored in the body for considerable periods of time. In most of these countries there are periods of fairly abundant supplies of vitamin A from leafy

vegetables followed by periods of short supply in the nonvegetable growing season

### ACCOMPLISHMENTS

It has been highly encouraging to note that following completion of the initial survey the countries have continued to carry out nutrition studies and have formulated and implemented practical recommendations that their own resources will enable them to carry out not just as an interim but as a basic program. Evaluation of improvement in the nutrition and health of a population is difficult. It usually is not of the dramatic type where the value can be determined immediately. Final evaluation of a nutrition program can only be made by measuring progress over the ensuing years, noting the general improvement in the health and vitality of the people and in the over all productivity.

**Korea** One of the first opportunities to evaluate the benefit derived from a nutrition survey came in 1956 when President Syngman Rhee invited the ICNND to conduct a resurvey of the armed forces of the Republic of Korea. The initial survey had been conducted in 1953 under the auspices of the U S Army Office of the Surgeon General by a team headed by Dr Harold R Sandstead.

The dramatic improvement in the nutritional status of the Korean soldier as noted on resurvey is illustrated by some typical data given in table 2. The inductee of 1956 was virtually indistinguishable from the inductee of 1953 with the exception of a better vitamin C nutriture. However there was a vast im-

TABLE 2 Imp m l f K 1956 mp d b 1953. All  
f g p p t g f t l b f m d f p on l m d

			1953		1956	
			R w	Afr 16 k g	R w	Af 16 w k g
Cal						
B I 90 pe	standard w	gh	27 0	46 0	29 0	26 0
90-110 p	ard w	ph	72 0	53 0	71 0	67 0
P oc						
L g d m			0	6 0		
S rum proe	6 g			11 0		
Tt m						
Calc d			4 0	4 0		
V a. C						
Sc rubt g			21 0	46 0		0 6
Se um	C 0 2 g/100 l		60 0	100 0	3 0	
V A						
F l ular k			3 0	13 0	5 0	4 0
Serum	min 4	20 µ /100 l		17 0		

provement in the nutritional status of the recruits after 16 weeks of training. It also was noted in 1956 that the longer the individual remained in service, the better his nutritional status became. These improvements were due, in considerable part, to the efforts of the Republic of Korea and the United States advisory personnel to carry out recommendations made following the 1953 survey.

As a result of the 1956 survey, it was decided that the refined wheat flour now provided by the United States will be enriched with 3.0 mg instead of 1.2 mg of riboflavin per pound. At the present rate of flour consumption in Korea, this will provide an increase of about 0.25 mg of riboflavin per man per day, at an additional cost of less than \$500 per 100,000 men per year.

An example of Korean ingenuity in developing a practical mess gear adapted to their type of foods is shown in figure 4.



*Figure 4. New mess gear developed by the Koreans for their army.*

**Iran and Pakistan.** The accomplishments of the nutrition teams to Iran and Pakistan in January to April 1956 have borne results far beyond expectations. Both governments, as expressed through their departments of defense, are extremely grateful for the nutrition studies and the assistance of our Military Assistance Advisory Groups. Nutrition services have been established and are carrying out the recommendations of the teams to improve the nutritional status of their troops. Since the departure of the United States nutrition survey team, the Iranian team has conducted a thorough appraisal of the troops located in the Khazh area, and additional surveys are under way. Iran also has rehabilitated a meat and vegetable canning factory and has plans



under way for a second food cannery. This has made possible the development and production of a canned, stew type field ration.

A quotation from the Health Director, United States Operations Mission, Pakistan, in the March 1956 issue of the *International Cooperation Administration Health Advisor* is noteworthy:

The entire program has benefited from the presence of an outstanding team of nutritionists furnished by the U S Interdepartmental Committee on Nutrition for National Defense. As a superbly organized action team doing large scale survey work with the Pakistan Armed Forces in several parts of the country, they have been able to reawaken interest in nutrition problems at all levels. By devoting long hours to intensive laboratory work and arranging discussions with key civilian and military officials in government, they have discovered several well qualified Pakistani bi-chemists and laboratory workers, some of whom eventually may form the nucleus for an effective national nutrition program.

*International Nutrition Committee.* As a result of contacts made by the United States nutrition survey teams in Iran and Pakistan, the Iranian government invited members of the Baghdad Pact to a general nutrition conference in Tehran in November 1956. The conference was attended by representatives of the Armed Forces of Iraq, Pakistan, Turkey, the United Kingdom, and the United States. The delegates passed a resolution recommending that an International Committee on Nutrition be organized on a permanent basis, with meetings to be held annually to discuss mutual nutrition problems. They requested the ICNND to serve as the secretariat for the first year of operation.

The United States Government, through the Departments of State and Defense, has authorized United States participation in the International Committee, and the governments of Iran, Pakistan, and Turkey have officially approved its formation. Plans recently were completed to hold the second meeting of the Committee in Turkey on 7-9 April 1958.

The hospitality of the Iranians, their sincere friendship, and the active participation of all delegates at the conference left a very favorable and lasting impression. This opportunity for discussing mutual nutrition problems, exchanging ideas, and learning of new techniques set a precedent for later meetings of this type.

*Turkey.* Although the nutrition survey was completed only a few months ago, it already is evident that the Turkish team members were of a high professional caliber and exceedingly well trained to continue an active and progressive nutrition program in Turkey. Within a few weeks after the United States team members had departed, the Turkish nutrition team conducted an addi-

tional survey of another area. They forwarded to the Committee detailed findings covering the clinical examinations, laboratory findings, and dietary and ration studies. Their reports show that their team is highly competent, not only in assessing the nutritional status, but also in formulating practical recommendations for improvement.

The preliminary report of the joint nutrition survey was reviewed with the Turkish survey team in October 1957. They had arrived at conclusions and recommendations similar to those of the United States team, and were actively investigating procedures and means for enriching wheat flour with riboflavin and increasing the fortification of margarine with vitamin A from the usual 400 to 500 I U per 100 grams to 8,000 I U, with establishment of Government specifications and controls to ensure such a level.

The laboratory equipment and supplies furnished by the United States are being used not only in support of nutrition surveys but also in furthering basic research on the effect of nutrition in reference to diseases and parasitic infestations. A comprehensive study is under way of the vitamin content of some of the principal foods, especially as concerns vitamin A, vitamin C, and riboflavin. The possibility of using locally prepared rose cale as a source of vitamin C is under study. (This is a product made from rosebuds that was used extensively by the German submarine forces in World War II.)

**Republic of China (Taiwan)** A report on "Rice Enrichment in Taiwan" was prepared by the ICNND and distributed to interested agencies, to implement the major recommendations for rice enrichment<sup>1</sup> that were made as a result of the nutrition survey of the armed forces of the Republic of China, conducted by the Office of the Surgeon General, U S Army, in the fall of 1954. This involved the establishment of two rice enrichment, (Premix) plants in Taiwan. These plants were purchased recently and will be in operation in the summer of 1958.

In this method of enrichment, 1 part of rice Premix, which contains supplemental thiamine, riboflavin, niacin, and iron, is added to 199 parts of rice at the local mills, where feeders meter the Premix into the stream of polished rice. The additional cost of rice enriched by this method is less than one tenth of a cent per man per day.

As an interim method, the Committee suggested and assisted in planning a test in Taiwan of a new means of rice enrichment, using an enrichment wafer that is added to the rice during cooking. Since the method of cooking rice in Taiwan does not involve the use of excess water, the loss of soluble nutrients is negligible. Also, the recipe and equipment for preparing rice are

uniform about 20 kilograms of rice are prepared in one pot. Each wafer contains 40 mg of thiamine, 120 mg of riboflavin, 600 mg of niacin, and 400 mg of iron, which enriches the rice at a level similar to that to be attained by the Premix procedure. The cost of the wafer method is approximately \$0.22 per man per year. A test completed in December 1955 indicated that the wafer method of enriching rice was practical in Taiwan and to avoid delay in improving the nutrition this method was implemented in 1956.

Use of enrichment wafers has the disadvantage of requiring close supervision, stringent control and co-operation by the mess personnel in the proper issue and utilization of wafers. Enrichment of rice is accomplished in thousands of mess halls whereas with the Premix method control points number only about 100. Also the wafer method is particularly suited for use only under normal messing conditions where standard batch quantities of rice are prepared.

**Goodwill Engendered.** Along with surveys that amalgamate scientific effort in numerous countries for the betterment of health and welfare many intangible benefits accrue although the mental and political responses as concerns goodwill, friendship and better understanding are much more difficult than the physical benefits to evaluate. The creation of good will and understanding has not been one-sided. Returning United States nutrition survey team members are doing "double duty." They are serving as individual ambassadors for the countries visited. Friendships have been created of much longer duration than just the three month tour. A part of what has been accomplished can be measured by the continued flow of correspondence exchanging scientific information, requesting technical advice on specific problems and reporting progress.

#### COMMENTS

**Opportunity for Learning.** Nutrition surveys in the developing countries afford an opportunity for experience and training personnel not only of the host country but also of the United States team in a wide variety of nutritional disease patterns. Concurrent with present day interest in the relationship of diet to heart disease, dental caries, cancer and other conditions the surveys present an excellent opportunity for further study of these problems. The program of the Committee anticipates conducting three nutrition surveys per year with a continued follow up in countries previously surveyed.

**Need for Nutrition Research.** The need for a more definitive practical laboratory method to assess riboflavin nutriture especially in populations that are subsisting on suboptimal or borderline intake of thiamine has been mentioned. The possible rela-

tion of low vitamin A intake to the incidence and severity of trachoma is of special interest in many areas of the world. A problem of considerable concern in the Near East is the high incidence of kidney stones. Is this of nutritional origin? Is the high incidence of parotid enlargement noted by Sandstead, Iohn, and Sessions<sup>2</sup> in Korea in 1953 of nutritional origin? This appears likely, since the incidence noted in the 1956 survey was markedly reduced.

In Libya a special nutrition condition was noted. The dietary intake of calories, riboflavin, thiamine, vitamin C, and vitamin A was at levels one would classify as suboptimal to deficient. There also was a high incidence of troops with low serum vitamin C and low levels of urinary excretion of thiamine and N<sup>1</sup> methylnicotinamide. However, the classical signs of active nutrition deficiency were present in only a relatively small fraction of the men examined. Based solely upon the physical findings, one would be obliged to interpret the data as indicating that no serious nutrition problems existed, but when the biochemical findings are considered together with the dietary intake studies it becomes apparent that nutrition problems do exist. These findings offer a challenge to nutrition researchers and emphasize the need for study in the field of suboptimal intakes of multiple nutrients and physiologic adaptation as related to health, work output, and resistance to disease.

**Reports Prepared by the Committee** The following reports on individual nutrition surveys and suggestions for corrective action have been prepared by the Committee, and a limited number of copies are available on request from the Executive Director, Interdepartmental Committee on Nutrition for National Defense, National Institutes of Health, Bethesda 14, Md.

1 Report on Mission to Near East, April 1955, by Dr. Frank B. Berry and Dr. Harold R. Sandstead

2 Trip to the Middle (Near) East, November 1956, by Dr. Frank B. Berry and Dr. A. E. Schaefer

3 Rice Enrichment in Taiwan, June 1955

4 Iran Nutrition Survey of the Armed Forces, Aug. 1956

5 Pakistan Nutrition Survey of the Armed Forces, Sept. 1956

6 Iran Nutrition Survey of the Armed Forces Supplement No. 1—The Khazsh Survey, Dec. 1956

7 Korea Nutrition Survey of the Armed Forces, April 1957

8 Philippines Nutrition Survey of the Armed Forces, Nov. 1957

9 Turkey Nutrition Survey of the Armed Forces Dec 1957

10 Libya Nutrition Survey of the Armed Forces and Civilians  
Dec 1957

### SUMMARY

The Interdepartmental Committee on Nutrition for National Defense was established early in 1955 by the Departments of Defense State Agriculture and Health, Education, and Welfare plus the International Cooperation Administration and (later) the Atomic Energy Commission. Its purpose was to deal with nutrition problems of technical, military and economic importance in certain foreign countries. Nutrition surveys have been made in Iran, Pakistan, the Philippines, Turkey, Korea and Libya on request from the governments of these six countries. Some 12 American educational institutions have released key personnel for the survey teams. The deficiencies most commonly noted were of riboflavin, thiamine and vitamin A and C to some extent of protein and total calories. Notable improvements in nutrition of armed forces personnel are being brought about by host countries through actions based on recommendations made as a result of the surveys.

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### WISE COUNSEL

Paul the apostle in his first epistle to the Thessalonians uttered the well known thought: Prove all things; hold fast that which is good. This counsel is particularly applicable to those who tend to worship the present and to scorn the past. The present may indeed represent the high immediate mountain view of medicine, but for all that the valleys of the past and the smaller mountain ranges that confine them are willy nilly part of the present. A more awareness of Greek, Hebrew, Arabic and Christian traditions as they relate to the present will give a physician a sense of pride in his calling and a feeling of being nearly complete in his total capabilities as he concerns himself with ethics, scientific education or patient-physician relations.

—From EDITORIAL

*New England Journal of Medicine*  
p. 290. August 8, 1957.

# RAPID SURVEY OF DELINQUENT SERVICEMEN

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**T**HE problem of the undesirable individual in service is a perennial one. Delinquent and recidivistic youths are a source of enormous expense and impediment to the Armed Forces. Efforts directed toward the rehabilitation and integration of these functionally antisocial persons are sometimes effective. Frequently, however, all measures that are offered or forced upon the man fail and at length his offenses lead to a discharge through court-martial (bad conduct or dishonorable discharge). Short of this his repeated petty offenses may lead to administrative separation for reason of unfitness (undesirable discharge) or unsuitability (general discharge). This is not meant to imply that an undesirable or general discharge is given in lieu of punishment; rather it is a convenience to the service in ridding itself of the unfit or unsuitable.

Observation of the course of many of these delinquents leads to the conclusion that it would be of considerable value to the service to be able to distinguish early between (a) the "hopeless" delinquent and (b) the type of deviant youth who might benefit by rehabilitation efforts and eventually effect an adequate service adjustment. A decision having been made the "hopeless" delinquent could be expeditiously removed from service. Such a decision, however, involves the danger of eliminating the potentially productive man along with the recidivist. Furthermore, there is no check on the decisions because future service adjustment—good or bad—has been precluded by the separation action.

Despite this pitfall there are many cases where careful scrutiny allows no other conclusion than that the individual is incapable of adequate adjustment. Although such men may not have completely exasperated authority or be on the eve of a court-martial, it is obvious that an unfavorable outcome is inevitable. For such cases, screening out procedures would be of considerable value to the service.

An approach to the problem of the undesirable individual in service that appears to be practical and economical is used in this division. In brief the method consists of the evaluation of all brig prisoners by the division psychiatrist with regard to their desirability. The initial problem in weeding out noneffective personnel lies in locating the suspected population and a ready-made group presents itself in the brig inmates. Although many undesirables will not be in the brig at any one time and others will never be in the brig at any time periodic surveys of all brig prisoners should establish contact with the bulk of service delinquents.

### METHODS

In arriving at his evaluation the psychiatrist uses four sources of information on the prisoner under consideration: (1) health record, (2) service record, (3) brig adjustment and (4) clinical interview. The first step is review of the health and service records, several areas being specifically noted. In the health record the pertinent areas are (1) previous psychiatric contacts and the results and circumstances of such contacts, (2) injuries sustained, this data often gives a clue as to the kind of violence and accidents in which the man has been involved, (3) physical profile (PULHES) changes, particularly the S (neuropsychiatric) factor, (4) venereal diseases and (5) rough estimate of the man's sick calls and the medication prescribed. The service record is examined in four areas, particularly (1) offenses and punishments, (2) promotions and awards, (3) proficiency scores at the time of enlistment and (4) transfers and reassignments.

These data often presented a telling picture of the service man's level of adjustment. The records readily revealed the men with the grossest failures in military adjustment as well as the men who had generally succeeded in service prior to the offense causing incarceration. The combined data arranged chronologically was useful in discerning patterns of maladjustment for inquiry in the clinical interview. For example, several years of unobtrusive adjustment may have been punctuated by a quick succession of offenses, or the man's periodic offenses may have been closely paralleled by the appearance of psychiatric and physical complaints, suggesting that his antisocial behavior is the acting out of a particular upsurge of psychological malaise.

The next step is a brief inquiry from the brig warden regarding the prisoner's brig adjustment. The warden's observations give a brief longitudinal picture of the man's adjustment in a rigid authoritarian environment.

The examination of the individual is completed with a clinical interview by the psychiatrist. The function of the interview is to supplement the available data in arriving at a decision on the

individual's fitness and desirability to the service. In many cases it is readily discernible that administrative separation from the service is not warranted. The interview might take only a few minutes to confirm the fact that the man has an adequate service record marred by a rare or single offense. An adverse decision recommending separation, requires more consideration. Occasionally two or three spaced interviews are necessary for complete evaluation. Psychologic testing is not used.

Interviewing brig prisoners proved to be surprisingly easy. Most prisoners regardless of clinical features, spoke readily in interview. Although many were guarded, evasive, or fearful it was rare to encounter a prisoner who did not respond in the interview. The non directive aspects of the clinical interview in juxtaposition to the brig routine and its extreme ban on interpersonal communication was a disarming experience to the prisoner. Many prisoners were anxious to communicate with the interviewer and expressed gratitude at the opportunity. Although the interviewer was aware of the manipulative aspects of psychopathic behavior the ease of communication in this setting remains a striking reality.

#### EVALUATION

The combined longitudinal and cross sectional data are evaluated and one of the following recommendations is made with regard to the prisoner's post incarceration status: (1) "Duty" meaning a return to full duty status following appropriate legal action; (2) "Duty Trial" meaning deferment of any existing action for discharge pending further trial at duty or retraining; (3) "Separation Unfitness," meaning it is recommended that the prisoner be administratively separated from service for reason of unfitness;<sup>2</sup> (4) "Separation Unsuitability" meaning it is recommended that the prisoner be administratively separated from service for reason of unsuitability,<sup>2</sup> or (5) "Treatment" meaning that where practicable, the individual will be treated psychiatrically within his command.

Where appropriate a clinical psychiatric diagnosis was made using the standard Armed Forces nomenclature. Where no noteworthy psychiatric symptoms or traits were manifest, no diagnosis was applied. On those men who received a recommendation of administrative separation a diagnosis of a personality disorder always was made. Alcoholism and other disorders sometimes were present. When a diagnosis of psychosis was made the man was removed from the punitive situation through medical channels. When a prisoner was recommended for administrative separation the psychiatric diagnosis of a personality disorder was used as a basis for listing in his health record the S (neuropsychiatric) factor of the PULHES profile<sup>4</sup> as 3 T (temporary).



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plete their tours, their actual functioning is often unproductive. They may complete "successful" tours only at great expense to the service in the form of hospitalizations, accidents, and legal and punitive actions. In addition, there is the effect of such men on the functioning and morale of their units.

The additional costs of utilizing marginal manpower have been demonstrated concretely in a number of follow up studies of the service careers of these men.<sup>6-8</sup> When marginally adjusted men were sent back to duty, the number of hospitalizations and disciplinary difficulties was several times that of their normal colleagues. Other studies have demonstrated that, where early psychiatric screening out is sparingly used, there is a substantially higher rate of psychiatric discharges at later stages.<sup>9</sup> Conversely, the liberal use of screening out procedures early in training is correlated with a reduced incidence of later psychiatric discharges.

The military psychiatrist is in a unique position with regard to available data. He is the only military person available who is equipped to evaluate all of the aspects of the total personality that must be considered: health record, service career, character structure, and psychopathology. The military psychiatrist is equipped to evaluate and synthesize the medical, military, and psychiatric facts present. The strategic use of the military psychiatrist in evaluating brig prisoners can be of high economic value in cutting short recidivistic careers and eliminating the legal requirements entailed in these careers.

The method has been described as it was applied in one Marine division. Obviously, it can be applied to any military service where a prison population and military psychiatrist are available.

#### SUMMARY

A method for the application of psychiatric survey to a pooled delinquent population has been described. The goal of this survey is to achieve the early elimination of undesirable personnel from military service before further expense is entailed.

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## DISCUSSION

Psychiatric screening out procedures for undesirable service men have not been accepted without question or criticism. It is pertinent here to consider some of the controversial aspects of military psychiatric screening. Glass and associates, in a detailed analysis of the screening process, compared predictions on 505 men made at induction with performance during their subsequent two years of service. The psychiatrist had predicted on a four point scale (above average, average, below average, poor) the adjustment of the man in three military zones (combat, combat support, rear). The authors showed that the psychiatrist tended to underestimate the performance of a psychiatrically handicapped serviceman. They found the psychiatric predictions to be poorly correlated with actual performance and pointed out that relying on psychiatric prediction for the elimination of undesirable servicemen would result in great manpower waste, many men being eliminated who would have been capable of completing their tour of duty despite psychiatric handicap.

There are significant differences between the method described and the wholesale screening of inductees. The latter may involve broad and elusive extrapolations. Not only does the predictor use past civilian adjustment to gauge future military adjustment, but also he may be called upon to consider several military environments in his forecasting. Extrapolations are minimized in the present method by two factors: (1) the available data and (2) the focus of the prediction. In the population here evaluated the individual had been in service long enough to attain a status of prisoner. He had had time to make some service adjustment and perhaps to form a set of attitudes toward the service. Many of these data are available to the psychiatrist.

It would appear reasonable that a prediction of future military adjustment would be more valid when based on past military adjustment than when based on past civilian adjustment. Furthermore, we are not concerned with vague or global predictions of adjustment. In the method described here, the important concern is limited to that of the disciplinary future of the serviceman, i. e. the *diagnosis of recidivism*. Psychopathology and the clinical picture, although useful in the psychiatrist's thinking, become secondary to this functional diagnosis. The question, "Will the man repeat his delinquency, if so, to what extent?" becomes the end point of the evaluation process and leads to the decision on his desirability. By the use of a specific focus and data that are highly relevant to military adjustment, the psychiatrist is placed in a position favoring the validity of his screening out decision.

The career of the psychiatrically handicapped serviceman deserves some comment. Although many such men are able to com-

plete their tours, their actual functioning is often unproductive. They may complete "successful" tours only at great expense to the service in the form of hospitalizations, accidents and legal and punitive actions. In addition there is the effect of such men on the functioning and morale of their units.

The additional costs of utilizing marginal manpower have been demonstrated concretely in a number of follow up studies of the service careers of these men.<sup>4-5</sup> When marginally adjusted men were sent back to duty the number of hospitalizations and disciplinary difficulties was several times that of their normal colleagues. Other studies have demonstrated that where early psychiatric screening out is sparingly used there is a substantially higher rate of psychiatric discharges at later stages.<sup>5</sup> Conversely the liberal use of screening out procedures early in training is correlated with a reduced incidence of later psychiatric discharges.

The military psychiatrist is in a unique position with regard to available data. He is the only military person available who is equipped to evaluate all of the aspects of the total personality that must be considered: health record, service career, character structure and psychopathology. The military psychiatrist is equipped to evaluate and synthesize the medical, military and psychiatric facts present. The strategic use of the military psychiatrist in evaluating brig prisoners can be of high economic value in cutting short recidivistic careers and eliminating the legal requirements entailed in these careers.

The method has been described as it was applied in one Marine division. Obviously it can be applied to any military service where a prison population and military psychiatrist are available.

#### SUMMARY

A method for the application of psychiatric survey to a pooled delinquent population has been described. The goal of this survey is to achieve the early elimination of undesirable personnel from military service before further expense is entailed.

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# CASE REPORTS

## Congenital Galactosemia

CLAUDE E BENNETT *Captain MC USA*

**T**HE CLINICAL syndrome of congenital galactosemia is now a well recognized entity with approximately 45 cases having been well documented. The relative rarity of this metabolic disorder in which normal physical and mental development can be expected with proper management prompts the following case report and discussion.

### CASE REPORT

An apparently normal male infant weighing 7 lb 4½ oz was delivered following a normal pregnancy. His father, mother, and one sibling were normal. Following delivery he received the usual care given newborn infants and was started on an evaporated milk formula. While in the nursery it was noted that his stools were loose and watery. Jaundice appeared the third day and persisted about two weeks. Due to the persistence of loose stools several changes in formula were made but without significant improvement.

At three weeks of age abdominal distension was noted. Because the loose stools persisted he was started at about four weeks of age on sulfaguanidine and his formula changed to skimmed milk and a banana preparation. There was slight improvement in the number and consistency of his stools but the abdominal distension became more marked.

The infant was hospitalized at one month of age at a civilian hospital at which time ascites was noted and an abdominal paracentesis was performed with removal of 30 ml of clear, light yellow fluid. At that time his hemoglobin was 10.2 grams per 100 ml and the white blood cell count was 39,750 cells per  $\mu$ l with a differential count of 2 per cent lymphocytes, 57 per cent neutrophils, 9 per cent band forms, 1 per cent metamyelocytes, and 7 per cent monocytes. Urinalysis revealed 2 to 3 plus albumin, 2 plus sugar, and numerous coarse and a few fine granular casts. The urine tested negative for bile and acetone. No hepatomegaly was noted at that time.

The following day the patient was transferred to this hospital. On admission examination revealed a pale, malnourished infant with slight puffiness of the face and eyelids and moderate edema of the sacrum, scrotum, and the lower extremities (fig. 1). The abdomen was obviously

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F. M. L. Sterman, Army Hospital, San Francisco, Calif. Capt. Bennett was assigned to 45th Field Hospital, APO 221 New York.

distended flank and shifting dullness were present. The liver was palpable 3 cm below the right costal margin. The superficial venous pattern of the abdominal wall was prominent. Examination was not otherwise remarkable.



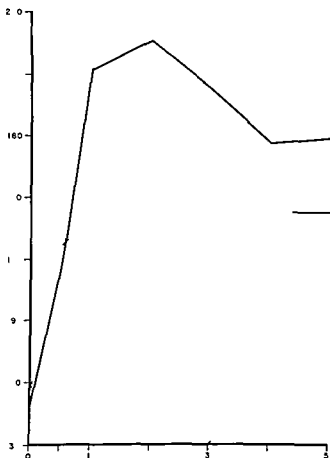
*Figure 1 Infant at one month of age prior to institution of therapy*

The initial laboratory studies revealed the following: hemoglobin 10.8 grams per 100 ml; nonprotein nitrogen 50 mg per 100 ml; creatinine 1.5 mg per 100 ml; fasting blood sugar 178 mg per 100 ml; total protein 3.4 (albumin 1.7, globulin 1.8) grams per 100 ml. Urinalysis revealed 4 plus sugar with no acetone. After fermentation with brewer's yeast, the specimen still tested 4 plus for reducing substance, and galactosazone crystals were demonstrated by the mucic acid and

osazone tests Roentgenographic studies revealed ascites but no other significant abnormality A large hematoma developed at the site of the femoral puncture

A tentative diagnosis of galactosemia was made and the patient was put on a milk free diet a soybean preparation being used Within 24 hours the urine was free of reducing substance Within four d ys the edema had disappeared The ascites had progressed however causing moderate respiratory embarrassment An abdominal paracentesis was performed with removal of 300 ml of straw colored fluid and the patient was given a transfusion of 75 ml of whole blood

The results of a galactose tolerance test followed by a glucose tolerance test for comparison are shown in figure 2 During the galactose tolerance test the patient's urine tested 4 plus positive for sugar whereas during the glucose tolerance test it was negative for sugar



Figur 2 Comparison of galactose and glucose tolerance tests.

The infant showed rapid improvement. After two days the ascites had disappeared and his weight was 6 lb 6¼ oz. Three weeks after therapy was initiated he weighed 7 lb 13½ oz; the liver had diminished in size but was still palpable and he was discharged to the care of his parents on a milk free diet (fig. 3). Follow up at four months of age three months after being put on a milk free (galactose free) diet revealed a normal infant (fig. 4). He has been continued on a milk free diet and at the last follow up at age 16 months he was reported to be normal with no evidence of mental retardation or other abnormality.

Galactose tolerance tests on the patient's parents and sibling were interpreted as normal.

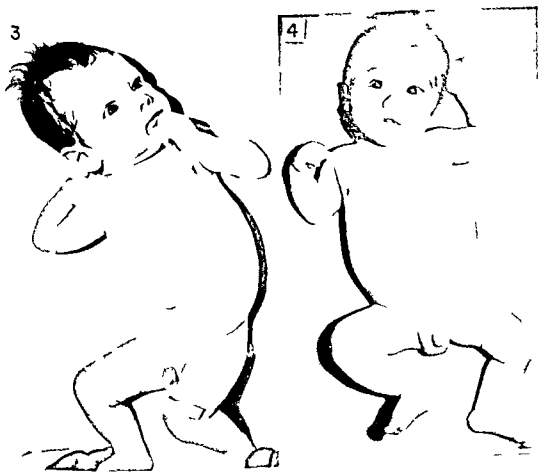


Figure 3 Infant three weeks after institution of milk free diet. Figure 4. Infant at four months of age.

#### DISCUSSION

This syndrome was clearly described by Gopport<sup>1</sup> in 1917, but the first case to appear in the American literature was reported by Mason and Turner<sup>2</sup> in 1937. A characteristic picture is now recognized, the most common features being failure to thrive, hepatomegaly, galactosuria, proteinuria, and aminoaciduria. Loss, commonly jaundice, vomiting and diarrhea, pyrexia, ascites, edema and hemorrhagic tendencies appear. If the patient is not



treated within the first 6 to 8 weeks cataracts and mental retardation become part of the clinical picture

The primary disorder in this condition is biochemical an enzymatic block in galactose metabolism that prevents galactose from entering into the regular metabolic pathways Schwarz and associates<sup>1</sup> recently showed that in untreated galactosemic patients there is a marked accumulation of galactose 1 phosphate in the erythrocytes Kalckar and associates and Isselbacher and co workers<sup>2</sup> confirmed the work of Schwarz and associates and were able to demonstrate that the basic defect is the lack of the enzyme phosphogalactose uridyl transferase which catalyzes the reaction in which galactose 1 phosphate reacts with uridine diphosphoglucose to form the nucleotide uridine diphosphogalactose They also demonstrated the presence of other enzymes necessary for the further utilization of galactose and its conversion into glucose 1 phosphate and thus into the regular carbohydrate metabolic pathway They concluded from their investigations that galactosemia represents the deficit of a single enzyme

Mason and Turner attributed most of the pathologic changes in this disorder to the low blood glucose level that is an accompanying feature They postulated that the low blood glucose level resulted in relative starvation of all tissues and eventual impairment of function of all cells of the body Mellinkoff Roth and MacLaggan questioned this hypothesis and were among the first to suggest the toxic effect of high serum levels of galactose Bruck and Rapoport pointed out that hypoglycemia from other causes such as von Gierke's disease and hyperinsulinism does not result in similar pathologic changes They considered the severe manifestations of galactosemia to be toxic effects of high blood galactose levels Other investigators<sup>3</sup> believe that the pathologic changes result from high blood galactose levels but that the exact mechanism is not fully understood The evidence seems to point to the direct toxic effect of galactose however competitive interference by high galactose levels with the availability of glucose for proper cell metabolism cannot be ruled out as a possible factor in the development of cataracts and mental retardation

Liver damage occurs early probably during the first week of life There are no pathognomonic changes but various degrees of parenchymal necrosis and fatty degeneration with consequent disorganization of the liver pattern have been noted In older children early hepatic fibrosis and fatty infiltration and in some cases typical cirrhosis have been observed<sup>2,4</sup> Early hepatic changes are reversible liver function improves and liver size decreases with the elimination of galactose from the diet<sup>2,5</sup> Cox and Pugh<sup>2</sup> stated that if the patient survives the critical early months of life liver repair occurs even

though galactose is not removed from the diet Hsia and associates<sup>9</sup> while concurring with the concept that the altered hepatic physiology results from the toxic action of elevated circulating galactose, pointed out that chronic loss of amino acids through the urine also will cause liver damage and cirrhosis.

Galactosuria has been shown by Cusworth, Dent, and Flynn<sup>11</sup> to occur as soon as the plasma galactose level is raised and to stop when the plasma galactose level returns to normal which suggest that galactosuria is due to the rise in the plasma levels of galactose. Komrower and associates<sup>10</sup> demonstrated that proteinuria, while not appearing promptly with the rise in the serum galactose level appears without fail within 48 hours following galactose feeding and increases steadily, with loss of substantial quantities of protein. The proteinuria diminishes rapidly following the elimination of galactose, and disappears after 4 or 5 days. Aminoaciduria occurs only after several days of high levels of galactose in the plasma, and disappears slowly over a period of several days after plasma galactose levels have returned to normal.<sup>10</sup> These studies suggest that the proteinuria and amino aciduria result from the toxic effect of galactose.

Holzel and Komrower<sup>9</sup> were the first to describe the presence of gross aminoaciduria in untreated galactosemic patients. Hsia and associates, using paper partition chromatography techniques demonstrated that the amino acid pattern is essentially similar in all cases, no single amino acid being excessively prominent. Both Hsia and coworkers and Komrower and associates, in similar studies, demonstrated that it was possible to restore the urine amino acid pattern to normal by offering a patient a galactose free diet, and to reproduce the abnormal picture by introducing sufficient amounts of galactose into the diet.

Donnell and Lann,<sup>12</sup> in a review of the literature reported four additional cases. They stated that in only one reported case and that one unproven has acetone been noted in the urine. Komrower and associates, in studying two infants with this disorder noted that both children showed the normal renal mechanism of acidification and had no significant alteration in the urinary excretion of sodium and potassium during the galactose feeding experiment. Also the blood urea was found to be within normal limits. The specific gravity of the urine varied considerably during this experiment and revealed ability of the kidneys to dilute and concentrate normally. They concluded that there is no permanent renal damage in patients with galactosemia who are properly treated.

Cataracts are a common finding in untreated and late treated cases. Ritter and Cannon<sup>13</sup> observed that infants in whom the diagnosis was made before they were six to eight weeks of age were free of cataracts or had minor ones that were reversible.

provided galactose was removed from the diet before the patient was three months old. Similar regression or disappearance of cataracts in infants who were put on a galactose free diet in early life and failure of regression in untreated patients or those treated too late has been noted by other investigators.<sup>1</sup>

Mental retardation appears to be the rule in the group treated late or not at all while infants put on a galactose free diet during the first six to eight weeks of life have shown normal development. Bain and associates<sup>1</sup> reported two cases in siblings one a slightly retarded child in whom the disease was diagnosed at four months. In the other the diagnosis was made in the first week of life and the child was normal. Mental retardation which is not reversible appears to be related to the duration of the untreated disorder.

Goppert was the first to note the familial incidence of galactosemia. In reviewing the 25 cases reported up to the end of 1952 Cox and Pugh again noted the familial incidence inasmuch as these 25 cases were from 17 families. Holzel and Komrower reviewed the literature on the cases with familial incidence proven and assumed and studied five cases in detail. Galactose tolerance tests were carried out on many relatives of these five patients. In each family at least one of the parents and many other relatives who had no clinical manifestation of the disorder were found to react abnormally to the galactose tolerance tests. They concluded that an abnormal galactose utilization as indicated by an abnormal tolerance test but without clinical manifestations is inherited as an heterozygous character while clinical galactosemia may be transmitted as a homozygous recessive gene.

### CONCLUSIONS

The diagnosis of galactosemia should be considered in any infant who fails to thrive, develops hepatomegaly and proteinuria and shows a reducing substance in the urine. The absence of acetone in the urine in the presence of 4 plus sugar suggests this disorder. Definite diagnosis is dependent on the demonstration of persistent galactosuria. High blood galactose, the characteristic galactose tolerance curve and the response to therapy are confirmatory. Due to the genetic factor any newborn sibling of a galactosemic patient should be studied during the neonatal period for galactose intolerance because it is possible to make the diagnosis at this time.

This is one inherent metabolic defect that can be treated satisfactorily. While the inherent defect remains, normal development can be obtained by the early exclusion of galactose-containing foods from the diet. The finding of a specific enzymatic defect suggests that a galactosemic patient should be continued indefinitely on an essentially galactose-free diet.

## SUMMARY

A case of the relatively rare disease, congenital galactosemia is presented to emphasize the urgent necessity for early diagnosis and appropriate treatment. Infants put on a galactose free diet before the age of three months develop normally whereas those not treated or treated too late suffer serious injury including liver damage, cataracts, and mental retardation

**ACKNOWLEDGMENT** The author is indebted to Private First Class James A. Akiyama for ultramicro method analyses carried out for galactose and glucose tolerance tests

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# Unusual Reaction to Local Anesthesia

## Gangrene of the Prepuce

EDWARD W. PINKHAM, Jr.    *Captain MC USN*  
ANDREW W. STEVENSON, Jr.    *Lieutenant MC USN*

**M**EDICAL LITERATURE is replete with reports such as that of Morrisset of systemic reactions to local anesthesia. Unfavorable local reactions have not been commonly recorded, however, and a case of gangrene of the prepuce following local anesthesia is worthy of comment.

### CASE REPORT

A 20 year old man was admitted to the hospital of this naval station for a routine circumcision. History revealed only difficulty in retracting the prepuce and therefore difficulty in maintaining cleanliness thereunder. There was no history of urinary difficulty or of peculiarity of the stream. Physical examination was normal except for the redundant prepuce which retracted with difficulty. After the customary preoperative studies, results of which were within normal limits, the patient was taken to the operating room where the pubic and penile regions were cleansed with phrisollex (brand of hexachlorophene) and draped with sterile drapes. The skin was infiltrated with 1 per cent Xylocaine Hydrochloride (brand of lidocaine hydrochloride) containing 1:100,000 Adrenalin (brand of epinephrine). The sites of injection were circumferentially at the level of the sulcus at the frenum and at both sides of the midline at the base of the penis. No excessive blanching of the skin is recorded.

Upon retracting the prepuce a minor degree of hypospadias and chordee was found at the base of the frenum. The hypospadias was corrected with chromic catgut sutures. The chordee was released. During this procedure the frenular artery was ligated in the distal frenum. The prepuce was replaced and a nonconstricting dressing applied.

The immediate postoperative course was not remarkable. The patient voided spontaneously with a normal stream. About 48 hours after the operation a dark red swelling of the dorsolateral aspect of the prepuce was noted. This progressed to bleb and vesicle formation and eventual gangrene of an area 3 cm in diameter. This area did not appear to be

one supplied by the frenular artery in its distal course. The remaining prepuce became edematous and dark in color but the reaction did not progress to gangrene. There was no evidence of secondary infection as exemplified by local pus or of systemic reaction as expressed by elevated pulse, temperature or white blood cell count.

Local warm wet dressings and prophylactic Terramycin (brand of oxytetracycline) produced subsidence of the edema and eventual separation of a black necrotic area on the dorsolateral aspect. When this area had healed a routine circumcision under Pentothal Sodium (brand of thiopental sodium) was performed. The patient returned to duty on the 6th postoperative day.

### DISCUSSION

Gangrene of the prepuce is uncommon. It can occur following neglected paraphimosis but has seldom been reported after local anesthesia, although Moore<sup>2</sup> stated that slough may follow in filtration of the prepuce. Because the method of infiltration used was a usual one, a review of the anatomy of the prepuce and of the action of local anesthesia containing Adrenalin was undertaken.

The prepuce is the integument of the penis reflected upon itself at the level of the sulcus.<sup>3</sup> Because the skin of the penis lacks adipose tissue it has difficulty in absorbing excess fluid from any cause. Its blood supply is derived in large part from the dorsal artery and must pierce Buck's fascia to reach the skin. The venous drainage is to the dorsal vein. This must pass through Colles' fascia. Both therefore pass through relatively inelastic tissue that could act to restrict blood flow. Because of the structure of arteries they are more likely to overcome this resistance than the veins, and under the proper circumstances they might produce an excess of fluid in the integument which the venous side could not relieve. This would add a further obstructive factor to the venous return that might be sufficient to cause the venous type of gangrene seen in this case.

Epinephrine produces vasoconstriction followed by a proportionate hyperemia.<sup>4, 5</sup> Southworth, Hingson, and Pitkin<sup>6</sup> believed that in dentistry most of the discomfort following local anesthesia is caused by this proportionate hyperemia in an area which is unable to cope with such an increase in fluid. These authors condemned the use of solutions containing 1:30,000 or 1:50,000 Adrenalin as being the cause of some of the untoward reactions attributed to the local anesthesia. They stated that a 1:200,000 dilution is adequate for hemostasis and does not cause subsequent unpleasant symptoms. Wilson<sup>6</sup> commented that 1:300,000 Adrenalin produced adequate hemostasis. As 1:100,000 Adrenalin was used in our anesthetic solution—strong enough to produce marked blanching of the skin of the oach—a marked

Representative Cole also said that it was his hope that the energy of the atom should like the reactor being dedicated forever be the servant and not the master of mankind. He told the audience that the reactor was being dedicated to the service of humanity and in so doing man's inventive genius was being directed to its highest purpose that of bringing relief from pain anguish and suffering.

The Under Secretary of the Navy the Honorable William B. Franke was a guest at the ceremony. Other speakers at the ceremony were the Honorable Dan Kimball former Secretary of the Navy and now President of the Aerojet General Nucleonics Laboratories San Ramon Calif. manufacturers of the reactor the Surgeon General of the Navy Rear Admiral Bartholomew W. Hogan Rear Admiral Thomas F. Cooper MC USN commanding officer of the National Naval Medical Center Captain Edward C. Kenney MC USN commanding officer of the U S Naval Hospital and Captain E. Richard King MC USN head of the Medical Center's Nuclear Reactor Project Committee.

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## Kimbrough Seminar Held at Walter Reed

The fifth annual James C. Kimbrough Urologic I Seminar was conducted at Walter Reed Army Hospital Washington D C 25-27 November 1957. Named in memory of the eminent Army urologist the late Colonel James C. Kimbrough the three-day meeting featured guest speakers from the military medical services as well as noted civilian doctors. The course director was Colonel John F. Patton chief of the urology service.

Civilian physicians who participated in the seminar included Doctors Roger Barker William P. Herbst Lloyd G. Lewis George E. Schreiner and Othmar C. Solnitzky of Georgetown University School of Medicine and Hugh J. Jewett and William W. Scott of Johns Hopkins University School of Medicine.

Colonel Kimbrough served as Chief of the Urology Service at Walter Reed from 1946 until his retirement in 1953. At that time after 36 years with the Army Medical Service he was designated by an Act of Congress as consultant in urology to Walter Reed Army Medical Center in recognition of his outstanding service and contribution to the science of medicine and surgery. He remained at Walter Reed in this capacity until his death on 19 August 1956.

## A MESSAGE FROM THE A M A

After nearly three years of planning, the Educational Council for Foreign Medical Graduates has placed an "open for business" sign on the door of its offices in suburban Evanston, Ill. The executive director of the Council, which will carry out a detailed and comprehensive program for evaluating foreign medical school graduates, is Doctor Dean F. Smiley, Chicago, Ill., former secretary of the Association of American Medical Colleges.

It was decided three years ago that some form of evaluation service should be established within an independent agency whose affairs would be directed by a board of trustees designated by four co-operating organizations, the American Medical Association, the Association of American Medical Colleges, the American Hospital Association, and the Federation of State Medical Boards of the United States. For the next two years, the Council will be supported by the four sponsoring agencies plus the Kellogg Foundation and the Rockefeller Foundation.

The Council, incorporated in the State of Illinois, will be administered by a 10 member board of trustees—two representatives from each of the four sponsoring agencies and two persons representing the public at large, one named by the U. S. Department of Defense and the other by the U. S. Department of Health, Education, and Welfare. The president of the board is Doctor James Murray Kinsman, dean of the University of Louisville School of Medicine, Louisville, Ky.

**How the Council Functions** Doctor Smiley said the Council will distribute to foreign medical graduates around the world authentic information regarding the opportunities and difficulties involved in coming to the United States on an exchange student visa to take intern or resident training in a United States hospital, or coming on an immigrant visa with the hope of becoming licensed to practice.

The Council will make available to properly qualified foreign medical graduates, while still in their own country, all information on how to obtain certification. This involves a three way screening process.

1. The Council will certify that a student's educational credentials have been checked and found meeting minimal standards—18 years of formal education, including at least four years in a bona fide medical school, but excluding hospital training.

2. The Council will certify that the command of English has been tested and found adequate for assuming an internship in an American hospital.

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From the Council on National Defense of the American Medical Association. This is a preliminary statement of the Department of Defense.

—Editor



3 The Council will certify that the general knowledge of medicine as evidenced by passing of the American Medical Qualification Examination, is adequate for assuming an internship in an American hospital

The Council also will provide hospitals, state licensing boards, and specialty boards which the foreign medical graduates designate with the results of the three way screening. It also will accumulate and publish each year complete data regarding the number and placement of foreign medical graduates in this country.

Doctor Smiley emphasized that the Council will not serve as a placement agency for either interns or residents; it will not attempt to evaluate the teaching program or inspect or approve any foreign medical school; and it will not act as an intercessor for foreign medical graduates having problems under discussion by state boards of medical licensure or specialty boards.

**First Examination in February** Doctor Smiley said that tentative plans call for the first American Medical Qualification Examination for foreign medical graduates already in this country to be held in either February or March 1958, and that the second such examination for foreign medical graduates both here and abroad will be held in either July or August.

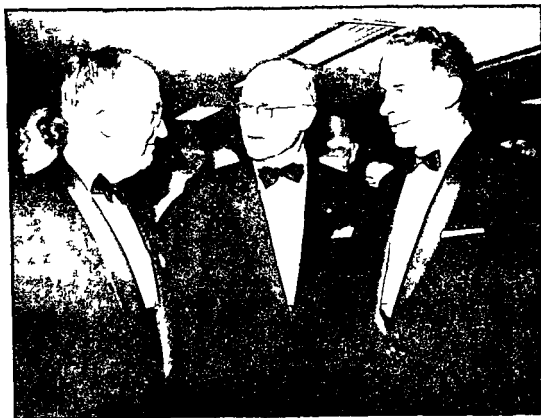
Formation of the Council was first announced last February at the fifty third Congress on Medical Education and Licensure in Chicago. It was the medical profession's answer to the mushrooming problem posed by the thousands of foreign trained physicians now in the United States.

In discussing the Council's work, Dr. Kinsman said that the screening process was initiated to help maintain the present high medical standards in the United States by making sure that foreign trained physicians wishing to come here for hospital appointments or practice have reached a level of educational attainment comparable to that of students in approved American medical schools at the time of graduation. At the same time, he added, the Council hopes to encourage the well trained foreign physician to take advantage of the opportunities to further his education in this country.

There has been a continuing influx of foreign trained physicians to the United States for a long time. At present there are more than 6,000 such physicians in this country on temporary visas serving as interns or residents. All foreign trained physicians here on temporary visas are supposed to return to their native countries on completion of their internship or residency training. In addition, there is another group of approximately 1,000 foreign trained physicians who enter each year as immigrants or as American citizens returning after completing their medical education abroad.

## DR BERRY GIVEN HONORARY FELLOWSHIP IN INTERNATIONAL COLLEGE OF DENTISTS

During the 12th International Dental Congress held in Rome in September 1957 the International College of Dentists conferred honorary fellowships on Doctor Frank B Berry Assistant Secretary of Defense (Health and Medical) Doctor John W Knutson Chief Dental Officer U S Public Health Service and Major General Oscar P Snyder USA Retired formerly Chief of Army Dental Service



*Left to right General Snyder Dr Berry and Dr Knutson*

The citations in recognition of services rendered the dental profession were presented to the three distinguished recipients by Doctor Frank F Lamons President of the International College of Dentists on 3 November 1957 just prior to the annual meeting of the American Dental Association in Miami Fla

In a concurrent meeting Colonel Roy L Bodine DC USA dental surgeon of the Fourth U S Army Fort Sam Houston Tex was elected president of the Academy of Implant Dentures A native of Indianapolis Ind, Colonel Bodine is a graduate of the State University of Iowa College of Dentistry in the class of 1924

## COLONELS MILLER AND ZAGELOW NAMED TO HIGH POSTS IN AIR FORCE MEDICAL SERVICE

Colonel Robert R. Miller USAF (VC) has been appointed Assistant for Veterinary Services in the Office of the Air Force Surgeon General and Colonel Leonard P. Zagelow USAF (MSC) is the new Chief of the Medical Service Corps according to a recent announcement by Major General Dan C. Ogle USAF (MC) Surgeon General of the Air Force.



Col. Miller



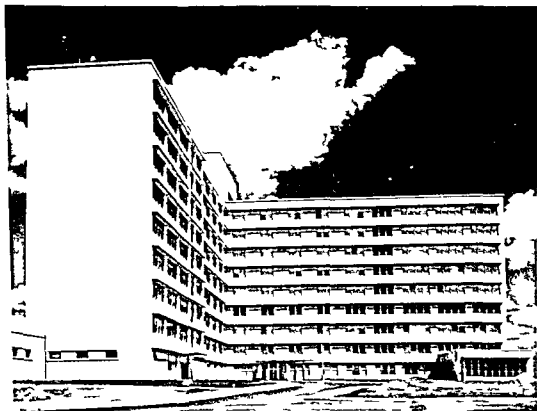
Colonel Zagelow

A native of Boston, Colonel Miller has been staff veterinarian of the Air Defense Command, Colorado Springs, Colorado, since graduating from the Air War College in 1952. Previously, he was veterinary staff officer in the Office of the Air Force Inspector General, Kelly Air Force Base, Texas. During the war, he served as a veterinary officer in Recife, Brazil, and later was attached to the Joint United States Brazilian Military Commission at Rio de Janeiro. He was graduated from the Ohio State University College of Veterinary Medicine in 1942.

Colonel Zagelow, who succeeded Colonel Phillip G. Fleetwood USAF (MSC), the first Chief of the Medical Service Corps, is a former infantry officer who transferred to the Medical Service in February 1938. He was graduated with a degree in pharmacy from Washington State College in 1937 and received his master of science degree from the University of Minnesota in 1951. In World War II, he was inspector of the 35th General Hospital in northern Luzon, P.I., and later executive officer for the Chief Surgeon, Headquarters Army Western Pacific, Manila. Colonel Fleetwood retired on 30 November 1957 after more than 30 years of military service.

## GENERAL OGLE DEDICATES NEW UNIT OF LARGEST AIR FORCE HOSPITAL

With the dedication of a new 500-bed facility on 16 November 1957 by Major General Dan C Ogle USAF (MC) Surgeon General of the Air Force Lackland Air Force Base Tex now has the largest hospital in major Air Force commands here and overseas Nearly 1 500 patients can be accommodated in the expanded treatment facilities Colonel John E Pluenneke USAF (MC) is commander of the hospital which is the key treatment center of the Air Training Command



*New Hospital at Lackland Air Force Base*

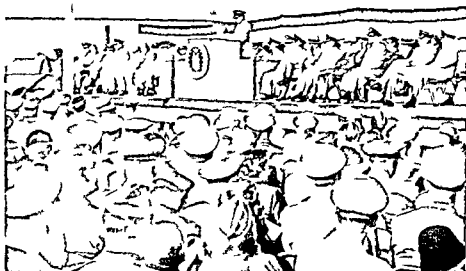


*General Ogle*

In his presentation General Ogle emphasized the growth of San Antonio as a leading medical center. He pointed out that in addition to the new Lackland Air Force Base hospital and Brooke Army Medical Center it is also the home of the new Air Force School of Aviation Medicine under construction at Brooks Air Force Base.

During the process of selecting a site for the new School of Aviation Medicine General Ogle told

the large audience of medical officers and civilian physicians and their friends a heavily weighted factor served to keep San Antonio from a position of unquestioned first choice. We believed and still believe that our new School and research laboratories should be in the neighborhood of a first class medical school that much could be gained by association between two such teaching and research institutions. There was no medical school here but San Antonio was finally selected because of many overriding advantages and because we had faith that this city would one day have its own medical school. I hope it will come in the near future. It is a community and national need that should not be denied.



General Grills welcomed distinguished guests.

Major General Herbert L. Grills, USAF, commander of Lackland Air Force Base, spoke briefly at the ceremony. General Ogle and General Grills were guests of honor of the San Antonio Chamber of Commerce at a dinner on the previous evening. Colonel James G. Moore, USAF (MC), is the surgeon of the Air Training Command, which recently transferred its headquarters from Scott Air Force Base III to Randolph Air Force Base.

The new hospital building, built at a cost of about \$9,500,000, was begun on 11 October 1954 and opened for the admission of patients on 16 September 1957. It contains 9 stories and basement of permanent masonry construction with accommodations for 500 beds. Under present plans, construction of an additional wing will start this year to provide an additional 500 beds for this large Air Force medical center. A total of 1,800 doctors, nurses, technicians, and administrative personnel is assigned to the center.

# OFFICERS CERTIFIED BY SPECIALTY BOARDS

## Supplementary Listing

According to information from the Offices of the Surgeons General of the military medical services, the following regular Medical and Dental Corps officers have been certified by the specialty boards indicated since the listings published in previous issues of this *Journal*

### American Board of Pediatrics

David W Davis Lt C 1 USAF

Wesly A Rads M J USAF

### American Board of Radiology

Charles F Krecke Capt USAF

### American Board of Internal Medicine

Lawrence R Loftis Capt USAF

Gerald I Mims M J USAF

### American Board of Preventive Medicine Public Health

Joseph W Cooch Lt Col USA

Robert W Sherwood M J USA

Arnold M Re M J USA

### Aviation Medicine

William O Bell Jr Lt C 1 USAF

William H Karmany Lt Col USAF

### American Board of Periodontology

Allan A Wallace Capt USN

### American Board of Prosthodontics

Alfred A Brainer Lt Col USAF

Myron C Turner Capt USN

William M Mink Cpt USN

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## DEATHS

ANDERSON Marvin Dale Captain USAFR (DC) of San Francisco Calif stationed at Chambley Air Base France graduated in 1956 from the School of Dentistry College of Physicians and Surgeons San Francisco Calif commissioned a first lieutenant in the United States Air Force Reserve 21 July 1956 ordered to active duty 8 September 1956 died 13 November 1957 age 28 near Solgne France as the result of an automobile accident

BRADY Richard Randall Lieutenant Colonel MC USAR of Miles City Mont stationed at the U S Army Garrison Southern Area Germany graduated in 1924 from the University of Nebraska College of Medicine Omaha Nebr commissioned a first lieutenant in the United States Army Reserve 7 January 1930 ordered to active duty 1 July 1942 died 1 May 1957 age 56 in Germany of coronary thrombosis

BROTHERS James William Second Lieutenant ANC USAR of Brooklyn N Y stationed at Fitzsimons Army Hospital Denver Colo graduated in 1954 from the Brooklyn State Hospital School of Nursing Brooklyn N Y served in an enlisted status from 19 January 1955 to 24 April 1956

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## Reviews of Recent Books

THE PATHOGENESIS OF CORONARY OCCLUSION by A D Morgan M A M D with a foreword by John B Duguid M D 171 pages illustrated Charles C Thomas Publisher Springfield Ill 1956 Price \$8 50

The first half of this book is an excellent review of the high points of the literature on a coronary artery disease and experimental atherosclerosis The later chapters present the material collected from 40 consecutive cases of advanced coronary disease in patients 47 to 80 years of age It is a discussion with excellent photomicrographs of histologic serial sections of the occluded portions of the arteries which he develops in support of Duguid's thrombogenic hypothesis of coronary occlusion This postulates that the typical lesion of atherosclerosis the subintimal plaque begins as a thrombosis in the lumen of the artery The arterial pressure flattens the thrombus against the wall The internal elastic lamina and endothelium layers grow from the margins burying the thrombus The subintimal thrombus is then organized by vasa vasorum growing in from the adventitia The cholesterol crystals from the stroma of enmeshed red cells are remnants of phagocytosis of the thrombus The inadequate vasa vasorum often hemorrhage into the plaque producing calcification and pressure atrophy of the media Inadequate organization of large thrombi result in the central softening termed atheromatous abscesses A vicious circle of abscess rupture with additional thrombosis leads to a layered structure of the plaque increasing the degree of occlusion The author implies that the lipid infiltration can at most be only a minor cause of plaque formation and suggests that the possibility of a relationship between fat metabolism and the coagulability of the blood is worthy of fuller investigation

—WILLIAM D PRESTON Col USAF (MC)

AN ATLAS OF CARDIAC SURGERY prepared by Jorge A Rodriguez M D 250 pages illustrated 10½ by 11½ inches in size W B Saunders Co Philadelphia Pa 1957 Price \$18

This atlas contains good technical information pertaining to surgery of the heart The first section begins with the anatomy of the organ in question There are 15 full page plates drawn by the author depicting the anatomy of the heart in situ as compared to the anatomy of the removed organ This is helpful to the surgeon in making his surgical approach to the heart With each of these anatomic drawings a written description of the anatomy as well as the surgical implications is presented The second part of the book presents several important adjuncts to cardiac surgery namely anaesthesia cardiac surgical instruments hypothermia and three types of mechanical devices used for extracorporeal circulation The drawings and the names of the instruments are of value to operating room technicians medical students and young physicians interested in cardiac surgery The four remaining sections deal with 29 recognized surgical procedures of the heart In



preparing these sections the author visited the clinics of 24 prominent cardiac surgeons and recorded their operative technic by firsthand observation

The author's observations are recorded in the book by legend and drawings. He describes the pathologic anatomy or congenital anomalies as the case may be giving the technical steps to repair the condition present. He also gives the anatomic or pathologic variations in the various conditions described. The legend begins with the positioning of the patient on the table and the location of the incision. For each figure in the legend there is a corresponding drawing illustrating the technical maneuver described. These are continued in sequence until the operation is completed. The author points out complications that may occur at the operating table and describes methods of prevention and control.

The work of Doctor Rodriguez is considered a valuable compilation of what is recognized as useful and possible to do in cardiac surgery at the present time. It should be available for the operating room technician, senior medical student and intern and in the library of the pediatrician and internist who study and refer patients for cardiac surgery. The resident in cardiac surgery will find it invaluable in mastering the present recognized technic in the specialty.

—LUTHER G. BELL, Capt MC USN

ORAL MEDICINE. Duguid, T. atmet by L. W. Burkett, A. B. D. D. S. M. D. S. D. with H. P. O. L. C. by S. G. D. C. St. G. L. B. A. B. S. M. D. F. A. C. S. 3d ed. 558 p. 391 ill. 11 tr. cl. dis. 40 b. t. n. ol. J. B. L. pp. c. tr. C. Phila. d. lph. P. 1957 P. \$14.

There is no doubt that this textbook is one of dentistry's classic contributions to professional literature. It is comprehensive without verbosity and its style is excellent.

The format makes this book remarkably easy to use, the text being divided into 12 sections which cover general considerations, diseases of anatomic regions and organ systems, occupational hazards, oral cancer, laboratory aids, a color atlas and a regional diagnostic index. The bibliography is extensive and well selected.

The author has an outstanding international reputation as a teacher and clinician and his wide experience has enabled him to utilize a large variety of illustrative cases. The text is well and profusely illustrated in black and white and in addition has a 40 plate color atlas presenting commonly encountered oral diseases.

This third edition has been extensively revised and in many sections completely rewritten to eliminate outdated material and to fully inform the reader on the most recent advances concerning oral disease. It is highly recommended for all students and practitioners of medicine and dentistry.—ARTHUR S. TURVILLE, Capt DC USN

TREVES SURGICAL APPLIED ANATOMY Revised by *Lambert Charles Rogers* V R D M D M Sc F R C S F R C S E F R A C S F A C S 13th edition 591 pages 202 illustrations 56 in color Lea & Febiger Philadelphia Pa 1957 Price \$7 50

The study of human anatomy can be a fearsome venture for some especially when presented in a weighty tome with a multitude of coded footnotes. But the mere size of this worthy little book makes the approach pleasant. It is not spectacular but basic and detail is used not as unrelated odd facts but as clinically helpful facts related to the anatomy of the part.

The chapter divisions are in the usual categories: *i. e.* "The Head and Neck" "The Thorax" "The Upper Extremity" "The Abdomen and the Pelvis" "The Lower Extremity" and "The Spine and Spinal Cord".

The format is simple and the use of boldface type in the paragraphical body brings forth to the eye the subject as clearly as the anatomy in a neat dissection. The index is likewise particularly clear and concise. The illustrations are mostly of simple line drawings, some in color and are spaced judiciously.

Frederick Treves' original purpose in the first edition of this book in 1883 was to give a precise basis to those incidents and procedures in practice that more especially involve anatomical knowledge and on the other hand endue the dull items of that knowledge with meaning and interest by the aid of illustrations drawn from common medical and surgical experience. Lambert Rogers has perpetuated those concepts and his revised edition should serve admirably as a handy friend for an intern or resident in surgery.

—RALPH M. MUGRAGE *Capt. MC USA*

CLINICAL APPLICATIONS OF SUGGESTION AND HYPNOSIS by *W. H. T. Heron* M A Ph D 3d edition 165 pages Charles C Thomas Publisher Springfield Ill 1957 Price \$3 75

This well written short monograph is a practical guide to the use of suggestion and hypnosis by members of professional groups. It describes in simple language the background and theory of hypnosis in direct relationship to its utilization as a therapeutic measure particularly in such fields as dentistry and obstetrics. Its primary aim is to encourage various therapists to use simple suggestion and the lighter stages of hypnosis to facilitate the treatment both for the patient and for the therapist.

Individuals who are adherents of hypnotherapy or who have a great deal of knowledge about hypnosis will find nothing new in this presentation. Neophytes in the use of hypnosis for professional treatment will find it easy to comprehend. The application of its principles however require careful study and supervision. The individual who would utilize hypnosis must believe in it himself. Suggestion or hypnosis a stronger and more complex form of suggestion achieves its ends

because of the affirmative interplay of subtle personal relationships which leads the patient to assume and accept that state of mind or attitude the therapist or hypnotist has decided is in the patients best interest. The author indicates that unless these technics are used to aid the patient they should not be used at all.

Hypnotherapy must be recognized as only one form of available therapeutics for the relief of all forms of the anxieties experienced by patients. For those interested in utilizing this type of therapy Dr. Heron's book represents a practical introduction which would best be followed by the examinations and study of other accepted publications on hypnosis. —LUCIO E. GATTO C I USAF (MC)

PRACTICAL REFRACTION by B m d C G tt M D 170 p ge ll  
t t d G un & Str tt l c N w Y k N Y 1957 P c \$6 50

The material in this manual represents personal experiences of the author gained through years of teaching and examining thousands of eyes. The arrangement of the material is somewhat unorthodox but it is presented in the manner the author believes most suitable to enable the refractionist to meet the patients actual refractive needs. Each chapter presents its subject in a reasonable and concise manner. Opinions and procedures are supported by clear reasoning and adequate explanations. The text dealing with Strum's conoid and ophthalmic lenses is especially valuable to those interested in these basic subjects.

There certainly are refractionists who will disagree with the author in the matter of managing hypermetropia. Commendably however he has emphasized that there are other effective methods besides his own for dealing with refraction problems. His only plea is that the refractionist know his subject, understand what he is trying to accomplish and work with thoroughness and accuracy. Emphasis is always on satisfaction from the patients standpoint. The occasional erroneous or obscure statement noted in the text in no way detracts from the manual which is well written, of excellent type and well edited. It is refreshing in its viewpoint and presentation and is highly recommended for both beginners and experienced refractionists who may be interested in doing a better job. —WILLIAM L. BERKLEY C pt MC USN

SCHIZOPHRENIA IN PSYCHOANALYTIC OFFICE PRACTICE Th Soc ty f  
M d l Psy h an ly t 1956 Symp m d t d by Alf d H R /k  
M D 30 cont b tor 150 p ge G un & S att l c N w York  
N Y 1957 P \$4

This book consists of the proceedings of a 1956 symposium of the Society of Medical Psychoanalysts on the office treatment of schizophrenia and contains all of the papers presented with the comments of the discussants. The papers in general fall into three categories involving the section on fundamental concepts of the nature of schizophrenia, special problems in treatment including transference anxiety and panic and the treatment of extramural schizophrenia including

methods of selection of cases and other similar considerations. All of the articles are stimulating and well worth reading. Naturally a book of this type is of great assistance to the specialist in the field of psychiatry. Unfortunately as one reads the points of view of the various authors and discussants one is more than ever struck by the fact that even among expert psychoanalysts with their considerable experience in diagnostic and therapeutic fields there is no general basis of agreement as to what in many instances constitutes an ambulatory schizophrenic. This defect in our nosology leads naturally to a considerable degree of variance in the approach to therapy in the diagnosis of the fundamental condition and in the handling of certain technical aspects of the psychoanalytic situation.

Some of the chapters particularly those on problems of negative transference, disliking one's patients, panic, suicide and the family role in ambulatory treatment are of particular interest to the individual who practices office psychiatry. There is also an interesting section on treatment of asocial attitudes in ambulatory patients which is well worth reading. As is usually the case, the publication of symposia of this type brings to the field fresh concepts and stimulates thinking concerning new approaches to old problems. This volume is well worth its relatively small price. —ROY E. CLAUSEN, J. Lt Col MC USA

**THE DOCTOR AS A WITNESS** by John Evans Tracy. 221 pages. W. B. Saunders Co. Philadelphia. 1957. Price \$4.25.

Because of the large number of civil court cases involving accidents or personal injury in which a physician is called upon to testify, this is a very valuable book to peruse beforehand. There are excellent descriptions of all the aspects of the doctor in the witness chair. He has certain privileges and certain obligations as a witness. He is very commonly called upon to give expert testimony which constitutes opinion evidence. There are chapters on the direct examination of the doctor witness and on the cross examination.

Insanity workmen's compensation proceedings and testimony in malpractice cases are reviewed. Stress is laid upon adequate preparation for trial or hearing and how to be a good medical witness. Proposed improvements in the law concerning expert medical testimony are included. This book is recommended for reading by anybody who has occasion to appear as a witness in court on either side of the disputed issue.

—FRANK P. GILMORE, Rear Adm. MC USN

**SYSTEMIC ARTERIAL EMBOLISM** Pathogenesis and Prophylaxis by John Martin Askey, M.D. 157 pages, illustrated. Grune & Stratton, Inc. New York, N.Y. 1957. Price \$5.75.

This brief monograph describes the various aspects of systemic arterial embolism. The early chapters discuss the problems of the risk, the morbidity and mortality and the clinical correlations of arterial embolism. Others consider the pathogenesis of cardiac mural thrombosis and systemic arterial embolism. Three chapters are devoted to

the diagnostic and prophylactic measures currently advisable in attacking the problem. The author has blended fact and theory into workable indications for and methods of treatment.

The book will be of value to the cardiologist the internist the general practitioner the general surgeon the cardiac surgeon the thoracic surgeon and the medical student as well as all practicing physicians. It is concisely written but covers the subject of systemic arterial embolism in an excellent manner.

—RALPH D. ROSS Capt MC USN

Collected Papers of THE MAYO CLINIC and The Mayo Foundation edited by  
 Richard M. H. White, B. A., M. A., M. D., J. H. R. M. E. B. A., M. A.,  
 Ph. D., M. Katharine Smith, B. A., Cal. M. Gambell, A. B., M. D.,  
 M. P. H. Fl. L. Schmidt, B. S., E. G. G. St. Iwell, A. B.,  
 M. D., d. G. v. White, B. A., M. A., Ph. D., Vol. 48, 1956, 778  
 pages, illustrated, W. B. Saunders Co., Philadelphia, P. 1957.

This is the forty eighth volume of the series of annual reports of the staff of the Mayo Clinic and Foundation and includes 712 new papers, 568 of which are referred to by title only. The book adequately covers most of the specialties and subspecialties of medicine and surgery. Many papers are presented in full, some by abridgment and others in abstract form. The editors have selected material appropriately and have presented it well. The papers are of general interest to all physicians. Some contain new information, others present different but well thought out views of controversial subjects and finally interesting case reports are included.

This book is recommended for all general medical libraries. The general practitioner will find it useful in keeping abreast of some of the newer developments (its coverage is compact and broad); the specialist will read to his advantage those sections relating to his own field and the remainder of the book he will find useful in keeping aware of the developments in the other fields of medicine. In this era of voluminous outpouring of medical writings, one finds it more and more necessary to resort to books which adequately abstract material in order to keep well read. This is one of those books.

—WILLIAM R. SCHILLHAMMER Maj MC USA

CLINICAL PHYSIOLOGY: The Functional Physiology of Diseases, edited by  
 Arthur Grollman, M. D., Ph. D., F. A. C. P., 854 pages, illustrated, The  
 Blakiston Company, McGraw-Hill Book Co., Inc., New York, N. Y., 1957,  
 P. c. \$12.50.

The great advances in modern medicine are a result of the application of physiologic instead of morphologic principles which were the bases for older clinical practice. No physician today can hope to practice or understand scientific medicine without a comprehension of the functional disturbance of underlying disease. This book meets admirably the long felt need for a text which presents the functional pathophysiology of disease. The editor with the collaboration of 25 eminent clinicians has presented the subject in a lucid and authoritative manner.

All the contributors are not only in active practice but also are well known for their research accomplishments. The book is divided into 33 chapters and 9 parts namely general metabolic considerations the cardiovascular respiratory digestive hematopoietic endocrine renal excretory locomotor systems and infection and immunity.

Through careful editing and pruning to which it obviously has been subjected this work does not suffer from the usual defects common in books of multiple authorship. It has been kept within the bounds of utilizable text. It is difficult to say that one section is written better than another. However certain chapters such as "Vitamins in Health and Disease" by Dr. William B. Bean were quite refreshing to the reviewer. The text is well balanced. The publisher's production and printing is commensurate with the high quality of the text. It is recommended to all physicians desirous of acquainting themselves with the scientific basis of medicine. The intern resident or practitioner preparing for his specialty board examination will also find the book of inestimable value. This text is ideal for the medical student to bridge the gap between the preclinical and clinical disciplines. The editor and his collaborators are to be congratulated for fulfilling this long-felt need in so practical and useful form.

—ARCHIE A. HOFFMAN Col USAF (MC)

ANNALS OF THE NEW YORK ACADEMY OF SCIENCES Volume 67 Art. 8  
pages 209-446 April 19 1957 Editor in-Chief Otto V. Schtelzel  
Viruses in Search of Disease 237 pages illustrated The New York  
Academy of Sciences New York N.Y. 1957 Price \$5

This paper bound volume consists of papers given at a conference held by the New York Academy of Sciences Section of Biology 24 and 25 May 1956. The chairman of the conference and consulting editor of this volume was Robert J. Huebner. Many notable names in virology are among the list of contributors. The contents are divided into five parts: Cocksackie viruses, new respiratory and ocular viruses, ECHO viruses, viral identification and classification, and criteria for etiologic association of prevalent viruses with prevalent diseases. The last part would have been better placed as an introductory section.

A volume of this kind is actually a glorified type of minutes. There is much repetition and overlapping in the papers given by many of the contributors. It is questionable whether conferences of this type should be reprinted in a book form. Many of the papers contained reports on work in progress, some were speculative, many contributions were essentially repetitions of previously published material. After reading this volume one is left with little practical information and internists who keep up with advances in virology are unlikely to acquire new academic information. The book's scientific merit is of course unassailable because the contributors are of America's most prominent virologists. However, since it is in substance only an edited record of the meeting, it is probably of little interest except to the participants of the conference. —ROBERT J. HOAGLAND Col MC USA

ANNALS OF THE NEW YORK ACADEMY OF SCIENCES V l m 67 Art 10  
 P g 671 894 M y 9 1957 Editor Chi f Off V St Wb t l k  
 M p bamar and O her Ag t Us d in M tal Disturbanc s 223  
 p g ill st t d Th N w Y l Ac d my f Sc s N w Yo k N Y  
 1957 P \$4

This book is a series of reports resulting from a meeting sponsored jointly by the divisions of biology and psychology of the New York Academy of Sciences in October 1956 The papers are divided into four sections Part one considers the chemistry pharmacology and mode of action of meprobamate and other agents and includes an article by Aldous Huxley The History of Tension which is well worth reading several times Part two contains five articles concerning treatment of psychoneurotic condition with various tranquilizing agents The authors of these articles are properly restrained in their enthusiasm for the drugs and repeatedly advise against indiscriminate usage Part three includes six reports on the treatment of psychiatric and other conditions with meprobamate These include chronic psychiatric patients senile psychosis postoperative surgical care alcoholism chronic headache and disturbed children The author of each of these articles report quite favorable results in treating the conditions discussed Part four presents a series of papers on the use of meprobamate in muscle spasm These include disorders of muscle tone muscle spasm due to rheumatic conditions skeletal muscle spasm cerebral palsy and the effect of meprobamate on basal ganglia (an experimental study on cats) The final report by R W Gurd summarizes the contents of the papers and could with profit be read first as well as after reading the other papers

This book is well organized The papers are easily read and include brief bibliographies and excellently edited discussions It is recommended for reading by clinicians —SAMUEL V THOMPSON Cpt MC USA

THE ELECTROCARDIOGRAM It is reported on Clinical Application  
 by L H Sgl M D F A C P F C C P F A C C 2d  
 dit s d 312 p g s Ill t t d Gun & Stetson I N w  
 Y k N Y 1957 P c \$8 75

This monograph on electrocardiography is a second edition of an earlier publication by the same author It is an improvement over the first edition but contains nothing original or different from the current texts on the subject of the electrocardiogram The chief purpose of this second edition as stated in the preface is to provide students taking an electrocardiography course with an up to date textbook and it is therefore of benefit primarily for those who are concerned with the author's program of teaching Although written as a recent edition the author continues to use such terms as auricular flutter fibrillation and tachycardia instead of using the more anatomic term atrial fibrillation flutter and tachycardia The discussions on the electrocardiogram after stress are very unrealistic

—THOMAS W MATTINGLY B & G Lt MC USA

**CRYPTORCHISM** by *Charles W. Charny M.D.* and *William Wolgin M.D.*  
 140 pages illustrated Paul B. Hoeber Inc. Medical Book Department  
 of Harper & Brothers New York N.Y. 1957 Price \$5.85

In all of urology there probably is no issue quite so controversial as that of the correct management of the undescended testis. In this monograph the authors attempt to reconcile the various viewpoints on the subject. This is accomplished by a comprehensive review of the literature and also by presenting the results of their own unique investigations of the problem.

All phases of cryptorchism are exhaustively reviewed including embryology, etiology, pathology, treatment and end results. Emphasis is placed on the essentialness of testicular biopsy as the only accurate method of functional appraisal in unilateral cryptorchism. The authors present the results of 132 biopsies done on testes which had been brought down previously by various methods and techniques and state that in practically every case the testis was incapable of normal spermatogenesis. This is ascribed to postoperative atrophy and/or congenital dysgenesis and apparently is independent of the method of treatment and the age at which treatment was carried out. Based on these observations the authors adopt a rather nihilistic attitude toward the problem of unilateral cryptorchism (notwithstanding the report of Gross & Jewett) at least until present methods of surgical management can be improved upon.

Although the authors of this work do not claim or attempt to write the final verdict on the management of the undescended testis, they do go a long way toward clarifying the basic issues involved and they very beautifully outline the path to be taken if order is ever to come out of the statistical chaos that now exists. There must be first accurate diagnosis, second biopsies of both testes during orchiopexy and finally follow up testicular biopsy when the child has passed adolescence. Not until this regimen is carefully followed out by all those willing to treat these patients will the final answer be known.

This is an excellent review of the problem of cryptorchism and should be read by anyone having occasion to diagnose or treat the condition.

—HOWARD POLLACK Capt. USAF (MC)

**DIAGNOSIS AND TREATMENT OF CARDIOVASCULAR DISEASE** 5th edition  
 in 2 volumes edited by *William D. Stroud M.D. F.A.C.P.* and  
*Morris W. Stroud III M.D.* Sixty contributors. Volume 1 chapters  
 1 through 29 pages 1 through 719 illustrated. Volume 2 chapter  
 30 through 53 pages 1001 through 1702 illustrated. F.A. Davis  
 Co. Philadelphia Pa. 1957 Price \$35 per set of 2 volumes.

This two volume work on the diagnosis and treatment of cardiovascular disease differs from the fourth (1950) edition in that loose leaf binding has been adopted to handle revisions and additions as the editors deem necessary. Although the book is not intended to be encyclopedic, it makes a comprehensive general reference of 53 chapters.



with an overlapping of subject material and the presentation of varying viewpoints. This can be confusing to the uninitiated student. In addition to the two editors there are 59 contributors who are authorities in their special fields of interest.

The following chapters on congestive heart failure, digitalis surgery of the heart and pericardium, coronary disease, disturbances of the heart beat and psychosomatic aspects of cardiovascular disease were found to be exceptionally well done.

The student who believes that he is fully cognizant as to the management of the problem of elevated blood pressure is referred to at least four chapters on that subject. The type and format used make for easier reading as compared to the previous edition. The section on vascular diseases, comprised of 10 chapters and is excellent as far as it goes. The references found at the end of each chapter enhance considerably the value of the book.

The book does seem to have the fault of so many texts with multiple authorship that is a change of place and viewpoint with the swing from the precise and affirmative to the indefinite and neutral. It is hoped the next revision will contain more data on vectorcardiography, phonocardiography and cardiac catheterizations. All in all this is one of the standard cardiology texts in American medicine and is recommended for inclusion in medical libraries.

—ARCHIE A. HOFFMAN C I USAF (MC)

BLOOD TRANSFUSION IN CLINICAL MEDICINE by P. L. M. H. M. D.  
M. R. C. P. 2d ed. 587 pgs. ill. t. c. d. Ch. I. C. Th. m.  
P. bl. h. Sp. g. f. ld. Ill. 1956 P. \$9

This volume is one of the most authoritative and readable I have seen on this subject. It is written by a doctor who has had many years of experience in the laboratory research phases of blood transfusions and also with a keen appreciation of the clinical aspects of blood disorders and blood utilization. The book has long sections devoted to laboratory technique including 61 pages on blood grouping. Approximately 100 pages describe blood incompatibility which is described as shortening of the life span of red cells by so antibodies found in either the recipient's or donor's plasma. This topic also includes 37 pages describing other unfavorable effects of transfusions.

The first chapter is concerned with the taking and storing of blood and the survival of blood components after transfusion. In this section the author states that purine nucleosides are being studied in the hope of preserving blood for longer periods but at present the rapid freezing of blood with glycerol will maintain red blood cells in good state up to 18 or more months. The rapid freezing technique must be combined with relatively rapid thawing when the blood is to be used. The freezing technique saves some space too because most of the fluid part of the blood is removed. One point of clinical interest in connection with

blood storage is the fact that hemorrhagic phenomena have been seen in patients after large transfusions of stored blood since a deficiency of platelets accompanies the infusion

The usual blood groups are described with the emphasis on the ABO system plus the Rh groups. However the chapter on the Rh system is very detailed and too complicated for most clinicians to understand fully. One very interesting chapter although quite detailed for the average physician is the one on estimating survival time of red cells in normals and in disease conditions. One practical point brought out by Dr. Mollison is to question the "universal donor" regarding any recent injections as some like hog pepsin may stimulate anti A bodies in the donor and consequently cause reactions in the recipient. It was mentioned that through studies with radioactive chromium in hereditary spherocytosis cells were taken up by the spleen while in sickle cell anemia the red blood cells are taken up by the liver primarily. Regarding thalassemia major the author reported that 50 per cent of transfusion cells were eliminated in five to nine days but a splenectomy in these cases reduced the transfusion requirements down to one third or one half of the previous requirements. The last two chapters consider normal blood findings in newborn infants, the placental transfer of antibodies and diseases of the newborn from the blood transfusion aspect. The book closes with 50 pages of references to world wide literature.

I recommend this book highly for every hospital or large clinic as it is an outstanding reference for internists, pediatricians and surgeons as well as of more frequent value for the clinical laboratory officer. —U. R. MERIKANGAS Col. MC USA

**BLOOD PRESSURE SOUNDS AND THEIR MEANINGS** by John Erskine Malcolm  
B. Sc. M. B. Ch. B. F. R. C. S. 93 pages illustrated Charles C  
Thomas Publisher Springfield Ill. 1957 Price \$2.50

This is a carefully written monograph on the physiologic mechanisms involved in the production of the sounds of Korotkov. Beginning with a review of past studies the author describes his own work using the superior fidelity of the cathode ray oscilloscope. The techniques described will be unfamiliar to most clinicians because they involve mathematical derivations. It is demonstrated that the sounds are caused by actual vessel excursions the nature of which is dependent on the principles of sound transmission through a system of nodes and nodes. Normally nodes are points where the arteries are physically fixed by fascial structures. Despite this careful presentation the meaning of these pressure wave sounds takes on no additional significance in terms of the clinical management of cardiovascular disease. The book's sphere of interest is that of the physiologist to the cardiologist or general physician.

—ROBERT B. DICKERSON

**SIGNS AND SYMPTOMS** Applied Physiology and Clinical Interpretation edited by Cyril Mitchell Ma Bryd A B M D F A C P  
3d edition 973 pages 191 illustrations 6 color plates J B Lippincott Co Philadelphia 1957 Price \$12

This volume is a collection of monographs by some 28 outstanding medical authors. As the title implies, the chapters deal with clinical manifestations of disease, their mechanisms, variations, and implications. The chapter headings include pain, headache, clubbed fingers, and hypertrophic osteoarthropathy, cough, hemoptysis, dyspnea, and fainting. The text is easily understood, well organized, and serves admirably the purpose of directing more attention toward the history and physical examination. This third edition has new chapters on growth and sex development, generalized vasospasm and arterial hypertension, and lymphadenopathy and diseases of the lymphatic system.

This is a real contribution to all clinicians. It is designed for ready reference and offers a physiologic approach to the understanding of symptoms and signs of disease. It is recommended to all physicians and medical students.—R J PEARSON J. Capt MC USN

**PROGRESS IN PSYCHOTHERAPY** edited by Julius H. Merman M D and J. L. M. M. D. Volume 2. Anxiety and Therapy. 264 pages. Gru. & Str. I. N. W. Y. N. Y. 1957. Price \$7.50.

This volume consists of selected papers by 28 contributors which were presented in the 1956 meeting of the American Psychiatric Association, augmented by articles written by various experts in the field. The book is divided into six major sections covering global psychotherapy, anxiety, special problems of stresses, schools, and trends in psychotherapy, developments abroad, and a summation.

The first part is thought provoking, yet one cannot help being left with the feeling that the creation of a therapeutic world order is in many ways impractical because, as with individuals, sick nations may be unable to be convinced even by the pressure of world opinion that they are in need of therapy. Of considerable interest throughout the entire book in all sections is the evolution of the importance of situational factors and cultural settings in the condition of the anxiety syndrome. It is obvious from the tone of many of the chapters that psychiatrists must direct more and more attention to the ecology of the syndromes which they are called upon to treat, particularly in psychotherapy.

Many of the papers presented are of outstanding quality. All are stimulating and well worth reading. Of particular interest is a section on developments of psychotherapy in foreign lands. It would seem apparent that the technical approach to psychiatric problems is gaining impetus in countries whose thinking in psychiatry is primarily oriented toward a more biopsychologic approach to mental illness. Anyone with psychiatric background and training will find this group of papers stimulating and will discover something of value in nearly all of them.

—ROY E. CLAUSEN J. Lt Col MC USA

THE YEAR BOOK OF NEUROLOGY PSYCHIATRY AND NEUROSURGERY  
(1956-1957 Year Book Series) Neurology edited by Roland P Mackay  
M D Psychiatry edited by S Bernard Wortis M D Neurosurgery  
edited by Osca Sugar M D 596 pages illustrated The Year Book  
Publishers Inc Chicago Ill 1957 Price \$7

This is a comprehensive condensation of the voluminous material recently added to the literature of the specialties of neurology psychiatry and neurosurgery There are reviews and follow up studies covering years of investigation for the busy doctor who is behind in his reading and there is indispensable material for the well read doctor who is staying up to date Outstanding authorities cover the various subjects The brevity of the material together with the numerous illustrations are assets of this Year Book

This book is indexed for quick reference by the general practitioner as well as the resident preparing for board examinations Its value is not limited to the specialist —JOSEPH J HORNISHER Col MC USA

FUNDAMENTALS OF GENERAL SURGERY by John Arnes Gius M D  
D Sc (Med) F A C S 720 pages illustrated The Year Book Pub-  
lishers Inc Chicago Ill 1957 Price \$12 50

This book is designed for the novice and represents the author's conception of the presentation of surgery at the undergraduate level The author is mindful of the magnitude of the medical field today and wisely omits details and confines his discussions to established principles and fundamentals essential to the proper comprehension and understanding of modern surgery based on sound physiologic and pathologic principles

One highly commendable and necessary feature of this book is a very complete and up to date bibliography at the end of each chapter Here the student is directed to specific articles or publications by recognized authorities which will supply the details necessarily omitted from the book For the practicing surgeon the book will prove a stimulating and refreshing review of modern surgical principles Particularly the early chapters should be most helpful in keeping the general man up-to-date in this rapidly advancing field As a desk reference book it is lacking in details however the fundamental principles are all there and well presented The book is full of pearls of wisdom briefly stated which will evoke a chuckle from the experienced surgeon but might be missed by the novice

It is realized that a line has to be drawn somewhere and that the author probably has very good reasons for omitting the genitourinary tract completely and except for injuries the bones joints chest and nervous system One wonders if for completeness these systems might have been briefly covered with profit However considering the obvious purpose of the book it is very well done and is a modern and refreshing approach to an old subject It would appear to be a valuable step in the right direction in adapting our undergraduate indoctrination to the demands of time and progress in the art of surgery

—PAUL E. SPANGLER Capt MC USN

CLINICAL PEDODONTICS by S d y B Fr D M D M S d 7 n  
 tr b t 664 p g ill t t d w th 275 f g w R B Sa d C  
 Ph l d lph P 1957 Pr \$12

This comprehensive textbook on dentistry for children offers dentists practical information in the care of younger patients. It presents the broad field in a clear and easily readable style. Among the chapters that have been included are parent counseling, child management, oral diagnostic procedures, the problem of pain and sedation, cavity preparation in primary teeth, pulp treatment and root canal therapy, fce development and tooth eruption, and preventive orthodontics and oral surgery for children.

The illustrations and tables presented are well chosen and are produced in an excellent manner. Particularly good are the tables listing disorders that affect the skull, the skin and hair, facial symmetry, the breath, lips, buccal mucosa, gingiva, tongue, tooth eruption, and occlusion. These and others offer a ready reference for diagnosis and treatment planning. This book is superior in quality and can be recommended for serious consideration to those who teach undergraduate students and to general practitioners who wish to keep abreast of the newer concepts and techniques in this broad field.

—GEORGE H. PARROT, J. L. C. I. DC, USA

ATLAS OF NEUROPATHOLOGY by Nathan M. Malamud, M.D. 468 p g s 226  
 p g s f pho g aph 2 p g f l pl t U r ty f Cal for  
 P e s B kel y 4 Cal f 1957 Pr e \$20

This atlas provides an extensive reference to the pathology of the nervous system. The author's work is well known to many students and graduates who have attended his classes in neuropathology or the review course he gives periodically for neurologists and psychiatrists preparing for the board examinations. The 10 chapters cover the gamut of pathologic conditions and include a chapter on cytology and cellular pathology which will help orient the reader to the special stains used in the nervous system. One chapter is devoted to the sequelae of perinatal and postnatal disorders. Dr. Malamud has been a United States Public Health Service investigator in the problems of cerebral palsy and is well qualified to discuss these often neglected entities.

There are 226 pages of photomicrographs. It is unfortunate that there are only two pages of color photomicrographs. The characteristics of the various entities are discussed and illustrative cases are presented on the pages facing the photographs, thus providing a quick synopsis of the condition being considered. The photographs include pictures of the gross and microscopic characteristics and various stains, and magnifications are used to illustrate typical lesions. Students and graduates will find this a most useful reference providing the most complete coverage available in neuropathology.

—ROBERT L. WILLIAMS, M.D., USAF (MC)

THE YEAR BOOK OF PATHOLOGY AND CLINICAL PATHOLOGY (57 Year Book Series) edited by William B. Wartman M.D. 510 pages illustrated The Year Book Publishers Inc. Chicago, Ill. 1957 Price \$7

The selection and abstracting of important articles in any medical specialty is not an easy task but Dr. Wartman and his staff certainly do an excellent job in the fields of pathology and clinical pathology. The abstracts are taken from articles published during 1956 and are, as in the past, grouped according to content under the various major headings (systems in pathology and subspecialties in clinical pathology). Dr. Wartman's analytical mind and keen sense of humor are repeatedly demonstrated by his numerous editorial notes and by the reprinting of a special article from *Lancet* entitled "On the Classification of Unicorns."

As in the past the publishers continue to use a good binding with high grade paper and have reproduced the illustrations in a clear and precise manner. This handbook can be recommended to all who are interested in keeping abreast of the times in pathology and clinical pathology. It is a must for all practicing pathologists.

—BRUCE H. SMITH Capt. MC USA

PSYCHIATRY IN THEORY AND PRACTICE by Beulah Chamberlain B.S., M.D. 150 pages Charles C. Thomas Publisher Springfield, Ill., 1957 Price \$4

The author of this small volume has achieved a clearly understandable coverage of present day psychiatric concepts. The reader experiences the feeling that he is listening to a highly competent, skillful and well-trained lecturer who knows the subject well and who speaks with the confidence of an authority. Dr. Bosselman has included a concise picture of the identifiable psychiatric entities with details as to historical origin, dynamic formulations, and differential diagnoses. As an added bonus the therapeutic goals are discussed. A notable omission, in my opinion, was the author's failure to discuss the use of electroconvulsive therapy in schizophrenia. Its use for the treatment of severely withdrawn or excited schizophrenics is still an old standby in many institutions in spite of the advent of tranquilizing drugs.

This volume provides enjoyable as well as authoritative reading and, even though the author's views may not always coincide with the reader's, it presents theories on specific aspects of psychiatric practice. I predict that one will be so impressed with the sincere and honest effort to cover the highly complicated problem of clinical psychiatry in such limited space that he will end up praising instead of criticizing. This book should prove to be particularly useful as an introduction to the study of psychiatry or for quick review. Psychiatric residents, psychologists, social workers, and physicians in general interested in psychiatry should find this book exceptionally valuable. —STEPHEN MOURAT Lt. Col. MC USA

A TEXTBOOK OF HISTOLOGY by Ale d A Max mu Lat Prof s t  
of An t my U e ty f Chi ag d W Ham Bl m P f s  
of An t my U i ty f Ch ag 7th ed t 628 p g 1 082  
ill st at 265 in c lo o 631 figur s W B Saund rs Co Ph l  
d lphia P 1957 P c \$11

This textbook is known to almost a generation of physicians and biologists as a standard reference. It was a new book when I studied it as a student in 1931 and the difference between that dog-eared copy and the current edition is instructive. This edition is some 100 pages shorter yet the number of the very excellent illustrations is almost doubled. The keynote of the text is found in the following quotation from the preface: "Vistas of the submicroscopic world have come into view and an exciting chapter is beginning with the fusion of some aspects of biochemistry and biophysics with histology." It is thus necessary to present medical students with an orienting text which not only describes the structure of the human body as seen with the optical microscope but which also considers relevant submicroscopic analysis and discusses function. This outlook has produced an admirable blend of the old and the new. This edition will be a required reference for all those who do serious microscopy at whatever level they may be in their educational process.

—WILLIAM D. TIGERTT Col MC USA

PHYSIOPATHOLOGY OF THE RETICULO-ENDOTHELIAL SYSTEM A Symposium edited by The Committee of the Organization of Medical Sciences under the joint auspices of UNESCO and WHO. Edited under the direction of B. N. H. J. P. B. B. A. / d J. F. D. I. / y 317 p g 11 tr t d Ch l s C Th m P b l h Spr g f ld Ill 1957 P c \$9

This symposium collected some of the most recent data on the reticuloendothelial system which includes phagocytic activity, metabolic function, and the role against bacterial infections. There are much detailed data of little use to the practicing pathologist but the chapters on morphology and physiology of the histiocytes, the role of the reticuloendothelial system in iron metabolism, and the means by which the reticuloendothelial system combats bacterial invasion and neutralize toxins bring together information which has come out piecemeal in the last few years. The data help to correlate morphology with physiology and create interest in the system which the clinical pathologist sees in his daily work. The work also emphasizes the need of re-evaluating and correlating our knowledge every so often in order to see how our concepts and definitions have broadened. What is the reticuloendothelial system? This symposium makes one realize that the definition is not so clear and that the limits depend upon who defines it. The book is written in English with the introduction and the resumes in French. It should be of interest to all physicians especially the internist and clinical pathologist and those working in both experimental and clinical medicine.

—PAUL C. LEGOLYAN Lt Col MC USA

## New Books Received

Books received by the U S Armed Forces Medical Journal are acknowledged in this department. Those of greatest interest will be reviewed in a later issue.

**BONE DISEASES in Medical Practice** by I. Snapper M. D. 229 pages with 24-page section of 48 plates. Grune & Stratton Inc. New York N. Y. 1957 Price \$15

**BONE TUMORS General Aspects and an Analysis of 2 276 Cases** by David C. Dahlin M. D. 224 pages illustrated. Charles C. Thomas Publisher Springfield Ill. 1957 Price \$11.50

**ORTHODONTICS Practice and Technics Companion Volume to Orthodontics Principles and Prevention** By J. A. Salzmann D. D. S. F. A. P. H. A. 497 pages 471 illustrations and 34 tables. J. B. Lippincott Co. Philadelphia Pa. 1957 Price \$20. (This book and its companion volume *Orthodontics Principles and Prevention* are available in a slip case at \$33 for the set.)

**ORTHODONTICS Principles and Prevention Companion Volume to Orthodontics Practice and Technics** By J. A. Salzmann D. D. S. F. A. P. H. A. 381 pages 262 illustrations and 26 tables. J. B. Lippincott Co. Philadelphia Pa. 1957 Price \$13. (This book and its companion volume *Orthodontics Practice and Technics* are available in a slip case at \$33 for the set.)

**ANNALS OF THE NEW YORK ACADEMY OF SCIENCES** Volume 65 Art. 6 Pages 653-1146 August 9 1957 editor in-chief Otto V. St. Whitelock. The Electrophysiology of the Heart. Conference Chairman and Consulting Editor Hans H. Hecht. 493 pages illustrated. The New York Academy of Sciences New York N. Y. 1957 Price \$4.50

**ANNALS OF THE NEW YORK ACADEMY OF SCIENCES** Volume 68 Art. 1 pages 1-244 August 30 1957 Editor in-chief Otto V. St. Whitelock. Proteolytic Enzymes and Their Clinical Application. Consulting Editor and Conference Chairman Gustav J. Martin. 244 pages illustrated. The New York Academy of Sciences New York N. Y. 1957 Price \$3.50

**ANNALS OF THE NEW YORK ACADEMY OF SCIENCES** Volume 68 Art. 2 Pages 245-656 October 21 1957 editor in chief Otto V. St. Whitelock. "Subcellular Particles in the Neoplastic Process. Consulting Editor Cornelius P. Rhoads. 411 pages illustrated. The New York Academy of Sciences New York N. Y. 1957 Price \$5

**ANNALS OF THE NEW YORK ACADEMY OF SCIENCES** Volume 69 Art. 1 pages 1-254 Sept. 7 1957 Editor in-chief Otto V. St. Whitelock. Biological Applications of Infrared Spectroscopy. Conference Co-Chairmen Robert P. Bauman and Carl Clark Consulting Editor Robert P. Bauman. 253 pages illustrated. The New York Academy of Sciences New York N. Y. 1957 Price \$3.50



ANNALS OF THE NEW YORK ACADEMY OF SCIENCES Vol m 69 Art 2  
 P g 255 376 A g t 30 1957 Ed t i -ch f Otto V St Whit k  
 Moder Id s Sp t o Ge t o Confe e Cha m d  
 C n lting Ed tor R F Ng ll 120 p g ll tr t d Th N w  
 York Acad my f Sc ce New York N Y 1957 P \$2 50

ANNALS OF THE NEW YORK ACADEMY OF SCIENCES Vol m 69 Art  
 3 P g 377 524 Octob 17 1957 ditor n hef Ott V St Whit  
 l k S o d C f c o S llon m d C lt g Ed t P rr  
 H L g 147 p g ill t d Th N w Yo k A d my f S c  
 N w Yo k N Y 1957 P \$3

ANNALS OF THE NEW YORK ACADEMY OF SCIENCES Vol m 70 Art 1  
 P g 1 152 A g st 30 1957 Ed t in-ch ef Ott V St Whit k  
 Th R l f l L bel d P o B l gy and M du Conf  
 Chairman d Con lting Ed tor S P M s d 152 p g  
 ll st t d Th N w York A d my f Sc N w York N Y 1957  
 P ce \$3

IMPLANT DENTURES Ind tson a d Pr du by Aa G h k ff B S  
 D D S d N ma I G ldb g D D S For w d by lrv g R H dy  
 D M D 256 p g 327 ll t t on d l olor pl t J B L pp t  
 C Ph lad lph P 1957 P \$12

GENERAL TECHNIQUES OF HYPNOTISM by A d e H W t h ff Ph D  
 460 pag Gu & St tt In N w York N Y 1957 P ice \$11 50

INTRODUCTION TO CLINICAL ENDOCRINOLOGY by A St art M M A  
 M D 192 p g Charl C Th m Publ h Sp ingf ld Ill 1957  
 P ce \$4 50

THE PRINCIPLES AND PRACTICE OF DIATHFRMY by By O S tt  
 M R C S L R C P D Phy M d 193 p g ll st t d Charl  
 C Th m s P bl h Spr gf eld Ill 1957 Pric \$5

THE INFANTILE CEREBRAL PALSIES by E C ll t l 100 p g  
 Charl C Th m P bl h Sp gf ld Ill 1957 P c \$3

QUANTITATIVE PHARMACFUTICAL CHEMISTRY by Gl L J k  
 Ph D J b E Chr t Ph D d G rg P H g Ph D 5th  
 d 552 p g ll tr t d Th Bl k on D on McG w H ll  
 B k C I N w Y k N Y 1957 Pr \$8 50

PUBLIC HEALTH NURSING PRACTICE by R th B F em R N Ed D  
 2d d t on W B S d rs C Ph lad lph P 1957 P \$5

THE PSYCHOLOGY OF GAMBLING by Edm d Be gl M D 244 p ge  
 H ll d W g I c N w Y k N Y 1957 P \$3 95

CLINICAL ORTHODONTICS A G de t th S t on l M hod by Be  
 F ch D D S 478 pag 1332 ll t at on on 354 f g es W B  
 Sa de Co Ph l d lph P 1957 Pr \$17

THE RETICULAR FORMATION OF THE BRAIN STEM A m al A p t  
 and F tional Co el ion by Al/ B dal M D Th ll d so T st  
 L t r P blic N XVIII 87 p g 23 ll st ion l d g  
 5 pl te P bl hed f Th W ll m R ms y ll d s T st by Ol  
 & B yd Ed burgh and Lond and Charl C Th m P bl h  
 Spr ngf ld Ill 1957 P r e \$3

THE DOCTOR EYES THE POOR READER by D lwy G S b b t B S  
 M S Ph D 101 p g s Charl C Th m s P bl h Spr gf ld  
 Ill 1957 P \$3 75

- CORTISONE IN DENTISTRY** by Lyon P. Streat M. Sc. Ph. D. D. D. S. F. A. P. H. A. 178 pages 57 illustrations Dental Items of Interest Publishing Co. Inc. Brooklyn N. Y. 1957 Price \$5.95
- AN INTRODUCTION TO ELECTROCARDIOGRAPHY** by L. Schamroth M. B. Ch. (Rand) M. R. C. P. E. F. R. F. P. S. 60 pages illustrated Charles C. Thomas Publisher Springfield Ill. 1957 Price \$2.50
- TECHNIQUE OF FLUID BALANCE** Principles and Management of Water and Electrolyte Therapy by Geoffrey H. Tovey M. D. 100 pages Charles C. Thomas Publisher Springfield Ill. 1957 Price \$2.50
- INTRODUCTION TO ANESTHESIA** The Principles of Safe Practice by Robert D. Driggs M. D. James E. Eckenhoff M. D. and Leroy D. Vandam M. D. 266 pages illustrated W. B. Saunders Co. Philadelphia Pa., 1957 Price \$4.50
- THE MICROBIAL WORLD** by Roger Y. Stanier Michael Duodoroff and Eduard A. Adelberg 682 pages illustrated Prentice Hall Inc. Englewood Cliffs N. J. 1957 Price \$8
- SYMPOSIUM ON NUTRITION AND BEHAVIOR** Nutrition Symposium Series No. 14 Proceedings of a Symposium held at the University of Minnesota School of Public Health Laboratory of Physiological Hygiene Minneapolis Minnesota April 27 1956 Josef Brožek Guest Editor The National Vitamin Foundation Inc. New York N. Y. March 1957 Price \$2.50
- THE PHYSICIAN'S OWN LIBRARY** Its Development Care and Use by Mary Louise Marshall American Lecture Series Publication No. 312 A Monograph in American Lectures in Internal Medicine edited by Roscoe L. Pullen A. B. M. D. F. A. C. P. 87 pages Charles C. Thomas Publisher Springfield Ill. 1957 Price \$3
- THE CHRONICALLY ILL** by Joseph Fox Ph. D. 229 pages Philosophical Library Inc. New York N. Y. 1957 Price \$3.95
- LABORATORY APPLICATIONS IN CLINICAL PEDIATRICS** by Irving J. Wolman, M. D. 1019 pages The Blakiston Division McGraw-Hill Book Co. Inc. New York N. Y. 1957 Price \$15
- BODY WATER IN MAN** The Acquisition and Maintenance of the Body Fluids by Maurice B. Strauss M. D. 286 pages 31 illustrations Little Brown & Co. Boston Mass. 1957 Price \$7
- PSYCHOLOGICAL DISORDER AND CRIME** by W. Lindsey Neustatter M. D. B. Ss. (psy.) M. R. C. P. 248 pages Philosophical Library Inc. New York N. Y. 1957 Price \$6
- SURGERY OF THE BILIARY TRACT PANCREAS & SPLEEN** by Charles B. Puestow M. D. Ph. D. (Surg.) 2d edition A Handbook of Operative Surgery 381 pages illustrated by Jessie W. Phillips The Year Book Publishers Inc. Chicago Ill. 1957 Price \$9.75
- HOST PARASITE RELATIONSHIPS IN LIVING CELLS** A Symposium Sponsored by The James W. McLaughlin Fellowship Program University of Texas Medical Branch Galveston Texas April 27 1956 Compiled and edited by Harriet M. Felton M. D. 245 pages illustrated Charles C. Thomas Publisher Springfield Ill. 1957 Price \$6.50
- DIGITALIS** Compiled and edited by E. Grey Dimond M. D. 255 pages illustrated Charles C. Thomas Publisher Springfield Ill. 1957 Price \$7
- ROOTS OF MODERN PSYCHIATRY** Essays in the History of Psychiatry by Mark D. Altschule M. D. 185 pages Grune & Stratton Inc. New York N. Y. 1957 Price \$5.75

THE HANGOVER A C ita l St dy th Psy h dyn mi f Al h li m by  
B jam K rpm M D 531 p g Illu t ti by W sley R W lk n.  
Ch l C Th m Publ her Sp gf ld Ill 1957 P e \$9 50

INTEGRATING THE APPROACHES TO MENTAL DISEASE Two Co fer  
H ld unde the Au p f the C mm tte o Publ H alth of Th New  
Yo k A ad my f M d ine edit d by H D Kuse M D 393 p g  
P l B H eb r l M d c l B k D p rtm t f H rp & Br th  
N w Yo k N Y 1957 P \$10

THE YEAR BOOK OF MEDICINE (1957 1958 Y ar B k Se s) S x Dep rt  
m ts. Part I f f t on by P l B B e M D. Part II Th Che t  
by C l M s b h m M D Part III Th Blood and Bl od F rm g  
O g s by W ll m B C tle M D P t IV Th H rt d Bl od  
V l and th K d y by T l y R H rr M D Part V Th  
D g ti System F a z j l g l f g M D and Part VI M c b l m  
by Ph l p K B dy M D 752 p g ill st t d Th Y r B k P b  
l her l c Ch g Ill 1957 P \$7 50

A DICTIONARY OF SCIENTIFIC TERMS Pr u c t D vation d D f  
i it f T rm i B ology B t y Z l gy A at my Cytol gy G  
tic Embryol gy Phys ology by l F H d o M A d W D  
H der M A B S Ph D F R S E 6th ed t by J H  
K m th M A Ph D F R S E F R S G S 532 p g D V  
N t d Co l Pr c t N J 1957 P \$12 50

THE GLAUCOMAS by H S ul S ga M D F A C S 2d d t 516 p g  
llu tr t d Paul B Ho b l c M d c l B k D p rtm t of H rp  
& B th s N w Y k N Y 1957 P e \$13 50

THE CLINICAL APPLICATION OF ANTIBIOTICS by M E Fl y M D  
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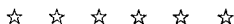
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## Monthly Message

Miss Catherine Letterman the eldest daughter of Doctor Jonathan Letterman for whom Letterman Army Hospital is named died on 14 October 1957 in her 94th year in the Presbyterian Hospital in Albuquerque New Mexico The Army and Air Force owe much to Doctor Letterman because he was one of three to rescue the Army Medical Service from its mire of hesitancy and inefficiency in the early days of the War Between the States As the war started the medical service was so unprepared and disorganized that the public demanded an investigation and President Lincoln appointed a Sanitary Commission to explore the whole problem The Commission insisted that former Assistant Surgeon William A Hammond then only 34 years old be appointed Surgeon General this was done in 1861

In 1862 Surgeon H S Hewitt U S Volunteers was the Surgeon for the Army of the Tennessee under General Grant and Doctor Jonathan Letterman was Medical Director of the Army of the Potomac Both independently had similar ideas as to the need for a complete reorganization of medical services in the field

In July 1862 Surgeon Charles E Tripler was succeeded in the Army of the Potomac by Assistant Surgeon Letterman who wrote at that time The Medical Department of the Army was in a deplorable condition He promptly reorganized the Medical Department of the Army of the Potomac and introduced system order and efficiency Although the Battle of Antietam occurred only three months after his appointment this was the first time in which all of the wounded were placed under shelter within 24 hours The organization planned by Doctor Letterman was the prototype of the present Field Medical Service of the Army and today's field evacuation and general hospitals and orderly evacuation of patients are not too different from what he organized

Miss Catherine Letterman and her younger sister Miss Madeline who survives now aged 90 lived in Washington for many years and Miss Catherine was the personal secretary of President Taft Secretary Brucker learned about the Misses Letterman

and wrote Miss Catherine a letter in early October expressing the interest of the Army and its gratitude for the enduring contribution their father had made to the Army Medical Corps. Ten days before her death Miss Catherine wrote the Secretary in appreciation for his letter.

*Frank B. Berry*

FRANK B. BERRY, M. D.  
Assistant Secretary of Defense  
(Health and Medical)

Since this article was written, Miss M. del. e. Letterman, 10, has died.

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## Foreword

The *United States Armed Forces Medical Journal* is the medium of dissemination of information of domestic and foreign military medical progress and of the Department of Defense. The Assistant Secretary of Defense (Health and Medical) and the Surgeon General of the Army, Navy, and Air Force Medical Officer and the Surgeon General of the Army, Navy, and Air Force Medical Officer are the authors of this journal.

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# UNITED STATES ARMED FORCES MEDICAL JOURNAL

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Number 2

## POSTERIOR COLPOTOMY

A Method for Diagnosis and Definitive Treatment

JAMES H. SMITH *Lieutenant Colonel MC USA*

JOHN B. NORTON *Major USAF (MC)*

**P**OSTERIOR colpotomy has long been recognized by gynecologists as a means of determining the presence and nature of pathologic conditions in the pelvis by direct visualization and palpation of the pelvic contents. The vaginal approach has been less widely used for definitive surgery, but in reviewing the literature<sup>1-4</sup> one discovers that in recent years more surgeons are advocating posterior colpotomy for both diagnosis and treatment of certain pelvic conditions. The reduced postoperative discomfort and hospitalization time have seemed to make this the approach of choice in many instances. The work reported here confirms the value of colpotomy in the diagnosis and treatment of a number of pelvic diseases.<sup>5</sup>

### MATERIAL

During the period January 1951 to January 1957, posterior colpotomy was performed on 47 patients at Colorado General Hospital. At Fitzsimons Army Hospital, between January 1955 to March 1957, 21 posterior colpotomies were performed. Essentially the same indications and technique were used at both hospitals, and all 68 patients are included in this report.

The age range of the patients was from 16 to 75 years. Some patients were nulliparous; the majority were multiparous.

### INDICATIONS

Colpotomy was selected as the procedure of choice for tubal ligation in patients who were not in the immediate postpartum --

*From Fitzsimons Army Hospital, Colorado General Hospital, Denver, Col.*

postabortal period. In patients with a suspected diagnosis of ectopic pregnancy, a posterior colpotomy with or without dilatation and curettage was made to establish the diagnosis and perform definitive surgery when possible. Colpotomy was not employed in cases where the diagnosis was obvious because of shock or loss of blood. Where bimanual examination was an inadequate means of evaluating pelvic pathologic conditions colpotomy with palpation and direct visualization of the pelvic contents was selected. In addition ovarian cystectomy and oophorectomy were done through the vaginal approach in many instances.

Previous surgery, endometriosis or previous pelvic inflammatory disease were not considered contraindications to colpotomy although it was known that abdominal laparotomy might have to be resorted to for definitive surgery. Age and parity were not considered contraindications. The indications for posterior colpotomy in these 81 patients were suspected ectopic pregnancy 40, elective tubal ligation 14, suspected ovarian pathology 14, unsatisfactory pelvic examination 7, and suspected endometriosis 6.

The procedures carried out through colpotomy incision were ovarian cystectomy 18, tubal ligation (Pomeroy technic) 14, salpingectomy unilateral 8, pelvic examination only 7, biopsy (endometriosis) 5, bilateral wedge resection ovaries 4, suture of ruptured bleeding ovarian cysts 4, oophorectomy (bilateral) 2, and oophorectomy (unilateral) 2. Dilatation of the cervix and curettage of the endometrium accompanied the procedure in 20 patients and abdominal laparotomy was resorted to in three patients.

## RESULTS AND DISCUSSION

The postoperative diagnoses in the 81 patients were diseased ovary 25, elective tubal ligation 14, ectopic pregnancy 10, no pathologic condition in pelvis 13, threatened abortion 6, incomplete abortion 5, endometriosis 5, and pelvic inflammatory disease 3. The average postoperative hospital stay for the patients in this series including the three who required laparotomy was three days. Similar procedures performed during the same period but by abdominal approach required an average hospital stay of seven days.

## TECHNIC AND PROCEDURES

The technic used is essentially that described by Bradbury. With the patient under conduction or inhalation anesthesia and in the lithotomy position the vagina was prepared in the usual manner. A weighted speculum was inserted in the vagina and the posterior lip of the cervix grasped with a tenaculum and elevated toward the symphysis. A transverse incision was made through the vaginal mucosa between the uterosacral ligaments. The vaginal

mucosa and the underlying fascial tissue were separated from the peritoneum by blunt dissection, and the peritoneum incised. By manual examination was performed with two fingers through the colpotomy incision, the entire pelvic contents being easily palpated.

The weighted speculum was replaced in the vagina with the tip in the vaginal incision. With the aid of thin right-angle retractors and ring forceps, the tubes, ovaries, and posterior surface of the uterus could be delivered into the vagina for direct visualization in most instances. If additional exposure was required, the uterosacral ligament and cardinal ligament was detached on one or both sides of the cervix and reattached on completion of the procedure. Salpingectomy, tubal ligation, ovarian cystectomy, and oophorectomy usually could be accomplished without difficulty. If extensive adhesions from previous surgery, inflammatory disease, or endometriosis prevented definitive surgery through the vagina, the incision was closed and laparotomy performed.

On completion of the procedure, the peritoneum, fascia, and vaginal mucosa are closed in one layer with interrupted sutures of chromic catgut.

In two patients with ectopic pregnancy, salpingectomy was difficult and the colpotomy was closed and a laparotomy was done. In the remaining eight patients with ectopic pregnancy the salpingectomy was completed through the colpotomy.

The patients with endometriosis diagnosed at the time of surgery had no surgical procedures done other than biopsy of the affected areas.

Ovarian cysts up to six cm in diameter were removed without difficulty or rupture, bleeding ovarian cysts were sutured. Bilateral ovarian wedge resection was performed as treatment for four patients with Stein Leventhal syndrome.

Patients with ectopic pregnancy or incomplete abortion had a dilatation and curettage at the same time as the colpotomy. In one patient, the diagnosis of pyosalpinx was made and laparotomy was performed to excise the involved tube.

Two patients, one with a ruptured ectopic pregnancy and one with pre existing pelvic inflammatory disease, developed pelvic abscesses postoperatively that required drainage through the previous colpotomy incision. Postoperative morbidity was present in the two patients who developed pelvic abscesses and in two other patients who were diagnosed as having pelvic inflammatory disease. None of the remaining patients had a temperature over 100.4 F after the first postoperative day. One patient was admitted two weeks postoperatively with a history of severe vaginal

bleeding but no bleeding point was observed and the patient was discharged without further treatment.

Patients were ambulatory within 12 hours of the surgical procedure without the usual postoperative discomfort. The average patient was discharged from the hospital on the second or third postoperative day and was back to normal activity at home within three or four more days. The chief postoperative complaint was mild shoulder pain that abated within 24 hours.

We prefer posterior colpotomy to culdoscopy because it permits better visualization of pelvic structures and is accompanied by minimal postoperative discomfort and hospitalization. Culdoscopy in our hands is cumbersome, discomforting to the patient and of limited diagnostic aid. Colpotomy has the added advantage of providing a satisfactory exposure for definitive surgery in some instances.

### SUMMARY

In 81 cases in which posterior colpotomy was employed the procedure proved to be valuable in the diagnosis of pelvic pathology while in many instances definitive surgery could be performed through the colpotomy incision. The hospital stay was reduced to an average of three days and the patients are more comfortable during the postoperative period.

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# POSTOPERATIVE PAROTITIS

## A Reappearing Disease

J VICKERS BROWN *Lieutenant MC USN*  
JOSEPH L SEDWITZ *Lieutenant MC USN*  
JOSEPH M HANNER *Captain MC USN*

THE INCREASED incidence of infections due to antibiotic resistant micrococci in hospitalized patients is reflected in the numerous articles recently devoted to this subject. Hemolytic *Micrococcus pyogenes* var *aureus* (*Staphylococcus aureus*) has been mentioned as a frequent offender. An unemphasized aspect of this problem is the reappearance of postoperative parotitis as a complication of surgery. As recently as 1955 this was referred to as a vanishing disease.<sup>1</sup> In one of the most comprehensive reviews of the subject, Coughlin and Gish<sup>2</sup> described the entity as encompassing all acute inflammations of the parotid gland except that occurring in epidemic parotitis or mumps. In this article only acute parotitis as it appears as a postoperative complication will be considered.

Even in the preantibiotic era the most common bacterial pathogen in surgical parotitis was *M pyogenes* var *aureus*.<sup>3</sup> Since the use of antibiotics has become routine throughout all phases of medical practice, many antibiotic resistant strains of this organism have appeared.<sup>3</sup> These resistant strains frequently are found in members of a hospital community. Detailed studies were made of the bacterial flora of the skin and nasopharynx of patients and personnel of Massachusetts Memorial Hospitals.<sup>4</sup> The predominant organism was found to be *M pyogenes* var *aureus*, hemolytic and antibiotic resistant and this finding was intimately related to an increased incidence of *M pyogenes* var *aureus* infected wounds noted in that institution.

## MATERIAL AND METHODS

**Frequency of Postoperative Parotitis** From 1 July 1949 to 1 July 1956 only 2 cases of postoperative parotitis occurred in 171,826 major and minor surgical procedures performed at this hospital. During the period of 1 July 1956 to 1 July 1957 47,947 major and minor surgical procedures were performed and there were 7



cases of postoperative parotitis. In the former period the incidence was 1 case of postoperative parotitis per 85 913 surgical procedures. During the past year the incidence was 1 case per 6 950 surgical procedures. This is a twelvefold increase in the incidence of this complication and is considered to be related to the general increase in the number of *Micrococcus pyogenes* infections noted here and throughout the country.

**Postoperative Wound Infections.** A moderate increase in the numbers of postoperative wound infections was noted on the surgical service of this hospital during the latter half of 1956 and early months of 1957. This coupled with the alarming increase in the incidence of postoperative parotitis noted during that period led to an effort to determine the carriers of the organism in the operating room and ward staff personnel. Cultures of nasopharyngeal secretions were performed on 136 personnel and 7 of these cultures were positive for *M. pyogenes* var *aureus*. The infectious agent was determined in 5 of the 7 cases of postoperative parotitis and was consistently *M. pyogenes* var *aureus*. Cultures were not performed in two cases because the process was recognized early and aborted by vigorous treatment. It is our feeling that the problem of postoperative infections is definitely related to the exposure of the patient to these antibiotic resistant micrococci carried by large numbers of hospital personnel.

### PREVENTIVE MEASURES

The prevention of this complication is empirical as the causative mechanism remains undetermined. The same measures that have brought about a decrease in the number and severity of postoperative wound infections can be expected to reduce the incidence of postoperative parotitis. Such steps as the exclusion of hospital personnel who are nasopharyngeal carriers from active ward duty and from operating or dressing rooms, the use of double masks during surgery, the changing of masks between cases, and the wearing of a mask and sterile gloves while changing a surgical dressing are time tested aseptic principles to which one should rigidly adhere, thereby reducing the incidence of infections in general. The previously accepted measures of oral hygienic care and stimulation of salivary flow are equally applicable today. Early diagnosis is essential. The examination of the parotid area should be included in the daily physical evaluation of the postoperative patient in order to allow early institution of vigorous treatment. Progression of the disease may be exceedingly rapid. One patient in this series presented only minimal swelling and tenderness in the parotid area with slight pain on mastication and 19 hours later the picture was one of full blown parotitis with massive facial edema and impending airway obstruction.

## TREATMENT

The treatment of surgical parotitis is basically the same as that of other infections. In the early case with minimal symptoms and physical findings, the stimulation of salivary flow induced by chewing gum or sucking on hard candy, the application of continuous moist heat and the use of massive doses of antibiotics has served to limit the infection. Our experience has led us to use erythromycin and Gantrisin (brand of sulfisoxazole) in combination, having noted that the greater number of *M. pyogenes* var *aureus* strains common to this hospital respond to these drugs though they are resistant to penicillin. Chloramphenicol also has been used with excellent results. In the present series x-ray therapy was used early in the treatment in five of the seven cases. One of the objections to radiotherapy has been that the edema secondary to radiation may prevent natural drainage of the infection through the parotid duct. It is our impression that drainage through the duct is so minimal as to have little or no effect on the inflammatory process occurring throughout the gland. We have noted that subsequent to irradiation the patients are both symptomatically and clinically improved. The patients received a total dose of 800 r in air, given over a four to six-day period with varying schedules of one to two treatments per day.

In the event that the previously mentioned measures fail to limit the infection, surgical incision and drainage of the gland is indicated. This should not necessarily be delayed until fluctuation is present. Due to the anatomic situation of the gland between fascial planes of the face and neck, marked necrosis can precede clinical fluctuation. Evidence of facial nerve paresis, impending airway obstruction or nasopharyngeal obstruction should be considered as absolute indications for immediate surgical intervention.

The technic for drainage that we have employed is carried out under endotracheal anesthesia. A curvilinear submandibular incision following the natural skin creases which may be extended to the preauricular area is used. After elevation of skin flaps, a hemostat is delivered through the tense capsule of the gland at multiple sites. An effort should be made to include the deep lobe of the gland and its preauricular extension in the area drained. If drainage is instituted early, one should not expect to obtain true purulent material but rather a cloudy fluid not unlike that found in early abscesses of the breast caused by *M. pyogenes* var *aureus*. The relief from pressure symptoms obtained by incision and drainage is gratifying and appears to limit the amount of necrosis that occurs. The wound is packed open and allowed to heal by secondary intention, despite which the cosmetic results have been satisfactory. Persistent salivary

fistulas have not been a problem in this series of cases. If airway obstruction is believed present, tracheotomy is performed at this time. In addition, a feeding tube is inserted through the nose to provide for postoperative alimentation. Postoperative care of the wound itself includes hot moist packs, frequent dressing changes, and daily irrigations with physiologic saline solution.

The following case reports briefly illustrate our experience with this problem.

### CASE REPORTS

C 1 A 35 year old man was admitted to this hospital for care and evaluation following a cerebral vascular accident. An arteriogram was made on 3 October 1956. Three days later swelling, tenderness, and pain on mastication were noted in the right parotid area. The patient was placed on 250 mg of erythromycin every four hours, but the swelling increased and there was marked toxicity. Surgical incision and drainage were performed on 13 October. Tracheotomy was required. Culture of the drainage revealed *Staphylococcus pyogenes* var. *aureus*. The patient's response to therapy was excellent, with complete resolution of the process by 10 December.

C 2 A 29 year old man underwent subtotal gastrectomy on 3 December 1956. His postoperative course was uneventful until 10 December when he developed an acute left-sided parotitis. He was initially treated with a combination of erythromycin and Gantrisin and received irradiation therapy. His facial edema progressed, however, and on 12 December surgical incision and drainage were performed. Partial airway obstruction was present, and a tracheotomy was accomplished at this time. The patient improved rapidly, and complete resolution of the process was noted by 7 January 1957.

C 3 A 60 year old man with partial obstruction of the large bowel was admitted to this hospital. On 13 December 1956 a left hemicolectomy was performed. On 26 December a transverse colostomy was accomplished because of a large leak along the anastomotic line. Two days later parotitis developed on the right, and the patient was treated with erythromycin, Gantrisin, and irradiation. Incision and drainage of the right parotid gland were performed on 2 January 1957. Parotitis of the left gland developed the next day, and the gland was incised and drained. The patient died 18 January of generalized peritonitis. The postoperative parotitis was believed to have been a major factor in his death.

C 4 An 18 year old youth, who one year previously had undergone a total colectomy for ulcerative colitis, was readmitted to the hospital because of recurring symptoms of partial obstruction of the small bowel. On 20 December 1956 he underwent lysis of adhesions, a segmental small bowel resection, and revision of his ileostomy. On 24 December

the patient had a transfusion reaction followed by oliguria and jaundice both of which receded over the next 10 days. On 6 January 1957 there was complete dehiscence of his abdominal wound which was closed the same day with through and through wire sutures. Two days later the patient developed a fulminating unilateral parotitis. Treatment with heat irradiation and 500 mg of chloramphenicol every six hours intramuscularly was begun but rapid progression of facial and cervical swelling necessitated surgical incision and drainage the same day. The parotitis rapidly responded and complete resolution of the process was noted by 15 January. The patient's course was progressively downhill however and he died on 2 March. Parotitis was not believed to have been a direct factor in his death.

**Case 5** A 52 year-old woman underwent radical mastectomy on 1 February 1957. A partial slough of both medial and lateral skin flaps was noted on 8 February. Secondary closure of the area with split thickness grafts was performed on 4 March. Minimal swelling pain and tenderness of the right parotid gland were noted the next day. Intensive treatment with erythromycin Gantrisin moist heat and oral hygienic measures was instituted immediately. Response to this treatment was excellent and complete resolution was noted by 11 March. This patient's illness was considerably lessened by early diagnosis and treatment.

**Case 6** A 54 year old man underwent subtotal gastrectomy on 26 February 1957. He had postoperative oliguria through 2 March 1957. Obstruction of the gastrojejunostomy was noted throughout the postoperative period. A partial wound disruption occurred on 6 March. On 25 March as the culminating factor of a very stormy postoperative course the patient developed parotitis on the left. This was initially treated with 500 mg of erythromycin every six hours and heat. Surgical incision and drainage were performed on 28 March. The patient died the next day. Surgical parotitis was believed to have been a definite factor in his death.

**Case 7** A 48 year old man underwent subtotal gastrectomy on 19 June 1957. Right parotitis occurred 3 days later and immediate treatment with heat irradiation and 500 mg of chloramphenicol intramuscularly every six hours was instituted. An excellent response with complete resolution by 29 June was noted. In this patient early diagnosis and intensive therapy was thought to have aborted the process.

#### COMMENTS

In reviewing this series of seven cases some general conclusions can be made. Postoperative parotitis occurs at varying intervals following initial or secondary surgical intervention. Although it may occur as a primary complication it more frequently occurs in combination with other surgical complications. Early recognition and extremely intensive treatment of post

operative parotitis minimize the morbidity associated with this complication

### SUMMARY

Postoperative parotitis is reappearing as a not uncommon and extremely serious complication of surgery. Its reappearance is thought to be related to the increasing number of carriers of antibiotic resistant micrococci (staphylococci) found in every hospital community. Measures designed to prevent this complication have been discussed and its treatment as carried out at this hospital has been illustrated by brief reports of seven cases. The early diagnosis of surgical parotitis has been found to be highly important in the successful treatment of this complication.

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### GOOD THERAPEUTIC TOOLS

Physicians who are not psychiatrists can do a great deal in helping patients in the psychological aspects of illness if they are aware that fundamentally sympathy, consideration, respect, support and understanding are as they always have been therapeutic tools of the greatest effectiveness.

—KENNETH E. APPEL, M.D.  
in *Journal of the Medical Association*  
of the State of Alabama  
p. 76, Oct. 1957

# EXFOLIATIVE CYTOLOGY IN THE DETECTION OF PELVIC MALIGNANCY

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**A**LTHOUGH vaginal and endocervical smears have been used for hormonal phasing in endocrine and menstrual problems and as an adjunct in the diagnosis of trichomoniasis and moniliasis, their greatest and most undisputed value is in cancer detection<sup>1-4</sup> With this in mind, we have analyzed the cytological smears obtained at this hospital from 13,501 patients during the two year period from 1 January 1954 to 1 January 1956

It has long been a policy in this hospital that all of our female outpatients and inpatients must have cytological smears taken at the time of examination, whatever the presenting symptoms The swab technic is employed, using cotton tipped applicators to take endocervical and vaginal smears After these patients are examined, they are advised to have a routine examination every six months, at which time cytological smears are again taken This accounts for many repeat negatives, because the same patient may have several negative reports

The situation in the military is unique We have no fixed patient load nor do we draw patients from any particular geographic area thus, many of our cancer patients are not seen initially by us, but are referred from installations and posts throughout the United States as well as from overseas Therefore, we cannot state that we have a certain cancer detection rate per thousand patients

In this study, all cytological smears were made by technicians who were unaware of the clinical or referred pathologic diagnosis This obviated the possibility of a prior diagnosis influencing the technician's interpretation of the smear

The classes of cytological smears and their significance are listed in table 1 On our service, Classes III IV, and V are considered positive, obligating us to make further diagnostic

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From Walter Reed Army Hospital Walter Reed Army Medical Center Washington, D C

studies Of 13 501 smears taken 260 were positive an incidence of 1 92 per cent It is our purpose to analyze the classification diagnoses and to correlate each classification with its corresponding tissue diagnosis The Class III smear although cytologically negative is significant enough to be considered clinically positive

TABLE 1 Classification of smears / Pap smear

Class	
I	Epithelial cells are normal in their appearance men trul history and clinical findings
II	Some typical cells are which are associated with non-neoplastic conditions such as parasitic and bacterial inflammations A repeat may usually equate when the infection has cleared
III	Borderline cells are seen which may be due to infection or malignancy The common denominator is morphologically atypical and proliferation of the epithelium in the process of which typical cells may appear
IV	Aiment of definite pre-invasive or early invasive highly typical epithelial malignant characteristics with metaphase in the term malignant characteristics and that the limited cells having characteristics are not necessarily associated with malignant possibilities
V	Grouped cells of markedly atypical hyperchromatic cells in which the required cytological criteria for malignancy and which are composed of malignant cells from primary site of malignancy are present

## RESULTS

Class V Table 2 shows that of the 260 positive smears 147 were Class V The distribution of diagnoses is also shown in this table On tissue examination 127 of the Class V smears (86 4 per cent) proved to be malignant whereas 20 were false positive although abnormal tissue was present in 19 of these A review of the cytology slides taken before biopsy studies showed that in the one patient in whom the cervix was reported to be normal the offending agent was trichomoniasis—a case severe enough to produce cellular changes which would result in a Class V smear There was a false positive rate of 13 6 per cent in the Class V Papanicolaou smears

Class IV Although the number admittedly is small there were 33 Class IV smears of which 13 were confirmed and 20 were not Their distribution is shown in table 3 In Class IV smears there was a false positive rate of 60 7 per cent

TABLE 2 *Diagnoses based on examination of tissue in 147 patients with Class V smear*

Class V (positive)		Class V (false positive)	
Squamous cell cancer of cervix	79		
Cancer <i>in situ</i>	26		
Adenocarcinoma of endometrium	12		
Adenocarcinoma of cervix	7	Cervicitis	12
Cancer of ovary (secondary)	1	Squamous metaplasia	3
Cancer of vagina (primary)	1	Cervicitis with basal hyperplasia	4
Choriocarcinoma (secondary)	1	Normal	1
Total	127		20

TABLE 3 *Diagnoses based on examination of tissue in 33 patients with class IV smear*

Class IV (positive)		Class IV (false positive)	
Squamous cell cancer of cervix	7	Cervicitis	9
Cancer <i>in situ</i>	4	Squamous metaplasia	6
Adenocarcinoma of endometrium	1	Cervicitis with basal hyperplasia	3
Adenocarcinoma of cervix	1	Leukoplakia	1
		Squamous papilloma in pregnancy	1
Total	13		20

**Class III** There was a total of 80 Class III smears. Twenty of these led to the diagnosis of malignancy and 60 were considered to be false positive (table 4). The false positive rate for the Class III smear was 75 per cent.

Table 5 is a composite of the foregoing material. From this table it is apparent that if one were to use only Class V smears when speaking of positive Papanicolaou smears, the incidence of false positives would be low because of the relative certainty with which this class has a tissue diagnosis of malignancy. On the other hand, while still being considered positive the Class III and IV smears do not have as high an incidence of malignancy.

When evaluating the results of vaginal cytology, one is impressed by the fact that its main use is in the detection of unsuspected carcinoma.<sup>4,6</sup> With this in mind, we reviewed all car-



TABLE 4 *Diagnoses based on examination of tissue in 80 patients with Class III smears*

Class III (positive)		Class III (false positive)	
Squamous carcinoma cervix	9	Cervix	41
Carcinoma uteri	6	Squamous metaplasia	13
Adenocarcinoma of endometrium	3	Cervix with basal hyperplasia	2
Adenocarcinoma of ovary	0	Leukoplakia	2
Carcinoma of uterine cervix (ectocervix)	1	Normal	1
Benign endocervical polyp	1	Endocervical polyp	1
Total	20		60

TABLE 5 *Summary of cytologic interpretation*

Class	Total number	Correct diagnosis		False positive	
		Number	Percentage	Number	Percentage
V	147	127	86.4	20	13.6
IV	33	13	39.4	20	60.6
III	80	20	25.0	60	75.0
Total	260	160	61.8	100	38.2

cinoma *in situ* cases in this two year period and the preceding three years to determine the number of cases detected solely by the Papanicolaou smear

In the clinical evaluation of the 84 patients on initial examination 37 cervixes were classified as normal in appearance and 32 showed erosion. Of the remainder diagnosis is not known in 7 while there was leukoplakia in 2 granulation in 2 easy bleeding in 2 necrosis in 1 and a polyp in 1. Of the 37 patients with cervixes initially classified as normal 3 were diagnosed and treated elsewhere. Papanicolaou smears from the remaining 34 showed 23 to be Class V 6 Class IV and 5 Class III.

We believe that these 34 cases exemplify the efficacy of Papanicolaou smears as a routine screening procedure in the detection of unsuspected cervical cancer. If for instance one or two quadrant biopsies had been made for screening purposes in these cases the area from which the biopsy specimen was taken would not necessarily have coincided with the actual cervical lesion. The material from a Papanicolaou smear represents a large surface and thus is more effective as a screening procedure.

## SUMMARY AND CONCLUSIONS

A review of the positive cytological smears seen during a two year period has been presented. In correlating the probability of malignancy as determined by cytological smear with the corresponding tissue diagnosis, we have shown that nearly 9 out of 10 patients with a Class V smear will have some type of genital tract malignancy while in those patients with a Class IV smear, the incidence drops to 4 out of 10, and in those with the Class III smear, to 2 or 3 out of 10. A five year study of carcinoma *in situ* revealed 34 instances in which a positive smear was the initiating step in establishing an altogether unsuspected diagnosis. Exfoliative cytology is not a diagnostic tool *per se* but it is a screening aid which warns the physician that further diagnostic procedures are necessary.

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## THE CARDIAC PATIENT FOR SURGERY

\*The clinician who evaluates a cardiac patient for surgery must first be convinced that there is a clear indication for operation. He must study the cardiac status and must estimate the operative risk. Once evaluation is complete and diagnosis made, a plan of management for the preoperative period, the actual operative procedure, and the immediate postoperative period can be outlined. In a number of instances patients with heart disease have coexistent conditions that necessitate surgical intervention. Many procedures, however, should be deferred until the physical condition permits operation with minimal risk.

—MAURICE G. DERANEY, M.D.  
CHARLES A. R. CONNOR, M.D.  
in *Heart Bulletin*  
p. 65 July-Aug. 1957

# CIRCULATING WHITE BLOOD CELL VOLUME IN LEUKEMIA

## Preliminary Report

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A NUMBER of laboratories have reported<sup>1</sup> that the red blood cell count and hematocrit may not be adequate indications of the status of an anemia. In multiple cases, the red cell volume, as determined by the use of cells labeled with radioactive chromium, has given a more reliable estimate of the space occupied by erythrocytes. Because of this, our attention was directed also to the white blood cell volume in comparison to the leukocyte count and its alterations in leukemia.

One criterion employed for following the progress of leukemia is the peripheral white cell count (number of WBC/ $\mu$ l). The end point of various therapeutic regimes has been a reduction of the white cell count to the normal range (generally under 10 000/ $\mu$ l). There is, however, little available information as to the response of the entire circulating white cell volume. On the basis of preliminary calculations herein reported, a normal value for the circulating white cell volume is established and changes during leukemia are documented. Possible use of this parameter in evaluating the response of intravascular leukocytes during the phases of leukemia is discussed.

## METHODS

Two techniques for determining the white cell volume were investigated.

**Red Cell Labeling** Red blood cells were tagged by the use of radiochromium ( $Cr^{51}$ ).<sup>2</sup> Fifteen ml of venous blood were added to a sterile rubber capped tube that contained both heparin and

50 microcuries of  $\text{Cr}^{51}$  in the form of  $\text{Na}_2\text{Cr}^{51}\text{O}_4$ . After gentle inversion, the tube was incubated at 37 C for 45 minutes. Plasma was withdrawn after centrifugation, and addition of sterile saline brought the volume to its original value. The washing was repeated twice and saline again added to reconstitute the volume.

Red blood cells are labeled with  $\text{Cr}^{51}$  by this technic. Leukocytes also take up the radioactive tag.<sup>1</sup> In normal individuals this presents no problem, because white cells occupy a volume of only about 10 ml (0.14 ml/kg of body weight, table 1) as compared with a total blood volume of 5 000 ml (71.5 ml/kg). In leukemia, the white cell volume is increased and the binding of radiochromium by leukocytes becomes a significant percentage of total  $\text{Cr}^{51}$  uptake. In order to avoid this, whole blood from leukemic patients was tagged with  $\text{Cr}^{51}$ , but only erythrocytes were used for reinjection into the donor. This was accomplished by discarding the upper "buffy" coat and washing the remaining red cells as discussed above. Three ml of the washed cells were kept as a standard and three were injected into the patient. Twenty minutes later, venous blood was withdrawn into a tube wetted with heparin, and a small quantity was employed in determining the hematocrit.

TABLE 1 *Calculation of normal white cell volume*

	Number per $\mu\text{l}$	Average radius in micro	Average volume in cubic micro s	Product of number c ll $\times$ radi <sup>3</sup>
Red blood cell	5 000 000	3.7	$\frac{4\pi}{3} \times 50.7$	$2.53 \times 10^8$
White blood cell	5 000	6.0	$\frac{4\pi}{3} \times 216.0$	$1.08 \times 10^6$
Rat RBC/WBC	$\frac{1 000}{1}$	$\frac{0.61}{1}$	$\frac{0.23}{1}$	$\frac{234}{1}$

$$\frac{\text{Volume RBC}}{\text{Volume WBC}} = \frac{234}{1} \quad \text{If RBC volume is 2 500 ml WBC volume is } \frac{2 500}{234} \text{ or 10 ml}$$

$$10 \text{ ml/70 kg body weight} = 0.143 \text{ ml/kg}$$

Three ml of the sample were counted in a well type scintillation counter, background corrected, and compared with the activity in the 3 ml standard.

$$\text{total blood volume} = \frac{(\text{corrected counts in standard}) \times 3}{\text{corrected counts in 3 ml sample}}$$

$$\text{white cell volume} = \text{total blood volume} \times \text{leukocrit or}$$

$$\text{white cell volume} = \text{total volume (red cell and plasma volume)}$$

**White Cell Labeling** Leukocytes, both normal and abnormal, bind radioactive chromium.<sup>3</sup> In theory it should be possible to incubate white cells with  $\text{Na}_2\text{Cr}^{51}\text{O}_4$  wash to remove unbound  $\text{Cr}^{51}$  and use the tagged cells in determining the leukocyte volume by the dilution principle. In practice however leukocytes are fragile and saline washing traumatizes the cells as observed under the microscope. White cell labeling appears to be the more direct approach but stabilizing materials such as proteins may have to be employed in the tubes to protect the leukocytes. Because of this, the red cell labeling technic was employed in the clinical cases.

### CASE REPORTS

**C 1** A 57 year-old Caucasian man was first admitted to the hospital 2 years prior to the present study because of generalized weakness and pain in the left upper abdominal quadrant. Splenomegaly was present. Peripheral blood cell counts and bone marrow aspiration established a diagnosis of chronic lymphatic leukemia. Hemoglobin was 7 grams/100 ml, platelet counts were within normal limits and the white count varied from 240 000 to 310 000/ $\mu\text{l}$ .

Initial treatment was with irradiation of the spleen and at the time of this study the patient was given therapeutic doses of radiophosphorus. Plotted in figure 1 are the peripheral white count and the white cell

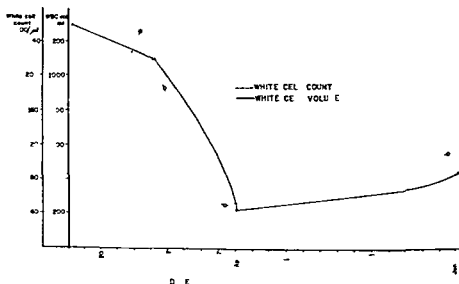


Figure 1. White blood cell count and white cell volume in case 1 (chronic lymphatic leukemia). Each x represents 1 millicurie of  $\text{P}^{32}$  used in therapy.

volume as determined by the red cell technic. Each x refers to 1 millicurie of  $\text{P}^{32}$  used in treatment. The initial white cell volume was 1250 ml (21.9 ml/kg) as contrasted with a normal value of 0.14 ml/kg. The

total blood volume was 5,400 ml (95 ml/kg) and the red cell volume was 950 ml (17 ml/kg). During therapy the white cell volume decreased to 225 ml (3.9 ml/kg). The total blood volume was 5,200 ml (91 ml/kg) and the red cell volume was 1,650 ml (29 ml/kg).

**Case 2.** A 43-year-old Caucasian man was admitted from another institution after a diagnosis of chronic granulocytic anemia had been established (white count 189,000/ $\mu$ l, bone marrow sample confirmatory). His initial complaints had been bleeding from the gums and night sweats. Splenomegaly and hepatomegaly were present. Hemoglobin was 11.5 grams. The platelet count and coagulation studies were normal. Initial white cell volume was 675 ml (9.9 ml/kg). Total blood volume was 5,100 ml of which the white cells represented 13 per cent. This can be compared with a normal situation in which white cells occupy 0.2 per cent of the blood volume. Following a total of 11 millicuries of  $P^{32}$  over a 2 month period the white cell volume decreased to less than 1 ml/kg and the white cell count fell to 8,800/ $\mu$ l.

### DISCUSSION

Numerically, white blood cells are only about one thousandth as abundant as red cells, but their volume, cell for cell, is nearly four times greater (table 1). In leukemia, the increased number of cells of the leukocyte series expands the white cell volume. Also, the abnormal leukocytes may have a volume quite different from normal cells. Hence the white cell volume may not increase in direct proportion to the leukocyte count.

In case 1, the white cell volume was 81.0 ml/kg, or 418 times greater than normal. Considering the magnitude of this figure, it is not surprising that white cells may approximate in leukemia.

The white cell volume generally paralleled the peripheral white count in the two cases presented. This is to be expected if the blood volume and average cell size remain unchanged. A distortion in either factor probably would result in discrepancies between the number of white cells per unit volume and the total volume of cells within the vascular tree. The picture is complicated in that many leukemic cells probably reside outside of the circulating blood and pass back and forth. It will be of interest to follow the circulating white cell volume in "aleukemic" phases and in the fulminating disease occasionally encountered in children.

Tagging of leukocytes appears to be the most direct approach in estimating the white cell volume. Although white cells accept the tag, they are fragile and often are damaged during the subsequent washing. One advantage of direct labeling of leukocytes is the fact that only small quantities of radioactive material are introduced into the body, and this can be readily cleared as white cells are broken down. When labeled erythrocytes are employed, their long survival time requires a determination of the blood volume a difficult task.

## SUMMARY

Determination of white blood cell volume by the use of radiochromium was accomplished by labeling red cells ( $\text{Cr}^{51}$ ) and determining the white cell volume from the difference between total volume and red cell plus plasma volume. Specific labeling of white cells is possible but has serious limitations. The normal white cell volume of a 70-kilogram individual was calculated on the basis of cell size to be 10 ml (0.15 ml/kg). In a patient with chronic lymphatic leukemia the volume was 1,250 ml (21.9 ml/kg). This fell to 225 ml during therapy with phosphorus 32 ( $\text{P}^{32}$ ). A patient with chronic granulocytic leukemia had a white cell volume of 675 ml (9.9 ml/kg) which decreased to normal following therapeutic doses of  $\text{P}^{32}$ . White cell volume generally paralleled the peripheral white cell count but there are possible causes of discrepancy and the use of this parameter in following the course of leukemia deserves further study.

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There can be no doubt that the hypoglycaemic sulfonamides will lower the blood sugar in many mild stable middle-aged diabetics. But the action of these compounds differs from that of insulin and although they may lower the blood sugar they need not necessarily correct the other metabolic disturbances of diabetes.

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# CLINICAL USE OF DIPHEMANIL METHYLSULFATE AS AN ANTIPERSPIRANT

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FRANK H. URBAN *Captain MC USA*

**P**RANTAL (brand of diphemanil methylsulfate) has been administered orally or topically in the treatment of various dermatologic conditions.<sup>1-4</sup> The results in control of sweating, contact dermatitis (dermatitis venenata), pruritus, urticaria, and dyshidrotic eczema generally have been favorable.

This report concerns the use of Prantal in concentrations of 2 per cent and 5 per cent in an inert powder vehicle for control of sweating alone and of diseases in which sweating accentuates an existing dermatitis. Ointment vehicles often tend to aggravate dermatologic disease especially in tropical climates, through their heat retaining and macerating effects.

The exact mode of action of Prantal when used locally is not known but it is believed that sufficient absorption takes place locally for it to act as an anticholinergic within the cutis, presumably by an effect on the most terminal cutaneous synapses of the parasympathetic nervous system. Certainly none of the systemic parasympathetic effects that would be expected from systemic absorption such as dryness of the mouth, dilation of the pupils, flushing, and diminished generalized body sweating were encountered.

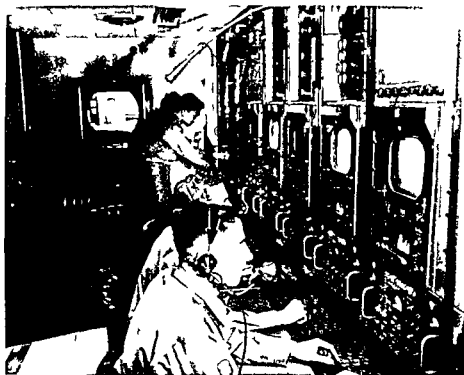
## MATERIAL

Sixty patients with various diseases of the skin in which primary or contributory factors were considered to be sweating were investigated. Fifteen other patients were lost to observation and are not included in this study. Concentrations of 2 per cent and 5 per cent Prantal were applied two to three times daily to affected areas without regard to type, location, or severity of the disease. Paired comparisons of 2 per cent and 5 per cent concentrations, commenced early in the study, were discontinued because many of the patients became confused as to

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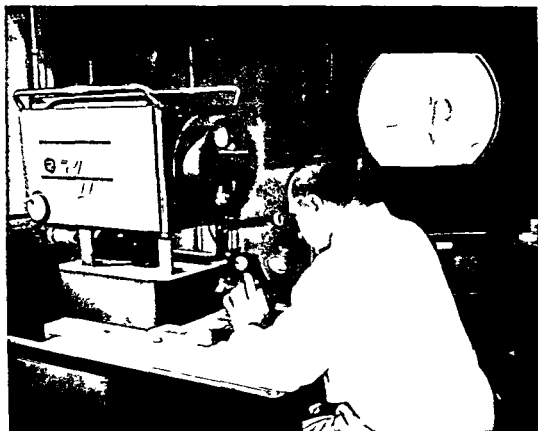
Figur 2 Room f m which f e colo came a b ads ar co troll d, thr e be g shown operation. Thi oom also ho s cod g systems t st i trum t emot ly controlled w th g lay and thr VHF tan m tt wh b f dth Cent r's xtens coaxial distribut o twork.

### TV MICROSCOPE CAMERA

One of the most unique pieces of equipment in the division is the color TV microscope camera mount (fig 3) designed by the Television Division in co operation with RCA engineers and built by the Biophysical Instrumentation Division of the Walter Reed Army Institute of Research. This system permits enlarged color reproduction on a TV screen from several types of stand ard microscopes enabling numerous scientists to observe study and discuss micro-organisms without taking turns viewing through a microscope. The entire assembly is mounted on rubber tired casters allowing it to be set up quickly wherever cable terminals are installed.

### OPERATING ROOM CAMERA

In one of the operating rooms a ceiling mounted color TV camera (fig 4) conveys close up views of surgical operations to Walter Reed students. The lens of this camera views the operating field via a mirror which reflects the surgeon's working area through a hole in the center of a light focused on the area. This camera mount can be turned a full 360 degrees and the



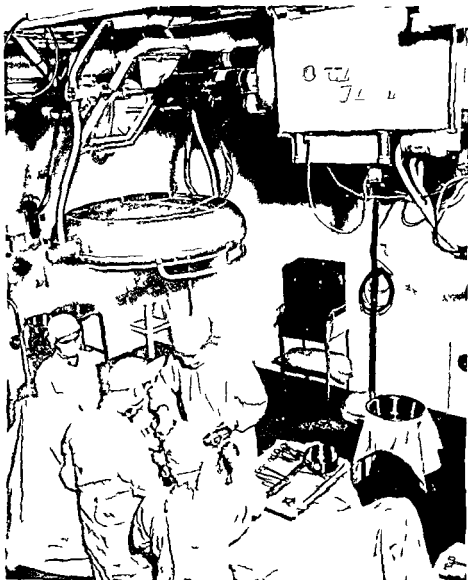
*Figure 3 This color TV microscope is completely new to the television industry. Light passes through the microscope and engages a beam-splitter which directs a sufficient amount of light to the microscopist's eye to permit him to examine suspect tissue just as though television were not involved. The remaining amount of light passes directly through the beam-splitter and is reflected through a prism into a three-vidicon color television camera of special design.*

camera can be moved on runners the length of the mount thus exposing all working areas in the room to view. In addition remote control of this camera eliminates the necessity for a television technician's presence in the operating room and prevents any interference with the surgeon. Seated in the control room an operator can focus the camera, select and change its lens, and follow action with tilt and pan controls.

#### AUTOPSY SUITE CAMERA

Similar to the operating room camera is another ceiling mounted camera in the McNabb Autopsy Suite at the AFIP. Thanks to this camera and its sister in the operating room, the difficulties of the operating room theater have been overcome. No longer is it necessary for a student to attempt to peer through the backs of operating room personnel or from a long distance, in order to glean some knowledge from the operation. Now he can sit in an auditorium or conference room and let television bring him a high quality color image of the operating area while the surgeon or

pathologist lectures through a microphone inserted in his surgical mask



Figur 4. C lo t l camera n operat g ro m qu pp d with a turret of le f varyi g fo al length. Th cam a look at th fac of a mure that i p nd d at a angl ab an ap t within the center of the operat g l ght w b ch alway i j d on the operati g f eld.

#### SURGEON PATHOLOGIST LIAISON

The operating room and autopsy suite cameras along with the TV microscope camera aid medical science. It is standard practice for a surgeon to send from the operating room to the

pathology laboratory through a panel. The certain tumors or diseased tissues removed from a patient. The pathologist examines the tissue and determines whether or not there is a malignant condition present. He then telephones the operating room and gives the surgeon the results of his analysis. With the aid of television, the pathologist can televise microscope slides of the tissue to the operating room and discuss it with the surgeon. He can also see the operating area himself since all this is done before the operation is completed.

### WRAIR CAMERAS

Two floor cameras in the Walter Reed Army Institute of Research studio facilitate programing from that building. Most dental surgery demonstrations are televised from here, as well as many programs on research and postgraduate education. By means of a telescopic lens on the camera, a single tooth can be enlarged many times to fill the entire 6 by 4 foot TV projector screen. One of these cameras can be moved anywhere in the building where cables are installed, and is sometimes moved to the hospital to back up the surgical camera there.

### TV PROJECTOR

When large audiences are assembled in Dart Auditorium at AFIP, Sternberg Auditorium at the Research Institute, or in the post theater they watch live color television as it is projected onto a 6 by 4 foot screen by one of the Division's two TV projectors. While throwing an image larger than can be viewed on a normal television receiver set, the projector loses none of the superior picture quality of the television screen and can be viewed by as many persons as can comfortably watch a television picture projection.

### TRINESCOPE

Medical officers stationed at Army posts throughout the world can keep abreast of the latest advances in scientific knowledge through films taken by the TV Division's color line trinescope known as the trinescope. This machine photographs television programs on 16 mm motion picture film in the same manner that appears on the television screen. Thus, any military installation that has access to a motion picture projector can receive the advantage of lectures, demonstrations given by some of the world's foremost medical authorities.

### PASI PROGRAMS

With this wealth of equipment the 50 civilian members of the Television Division have aired over 100 programs since July 1956. These included not only showings viewed locally over the Walter Reed channels but also many piped to downtown locations in Washington.

to New York City. The latter was a two hour dental demonstration micro waved to a meeting of the Greater New York Dental Society. Recently Walter Reed scientists presented professional papers to members of the Medical Society of the District of Columbia at Washington's Statler Hotel over closed circuit television emanating from Walter Reed. Medical men attending the October meeting of the Association of Military Surgeons of the United States saw live television demonstrations over Walter Reed's TV facilities. Working with the University of Maryland the Division is producing a series of advanced mathematics courses for teachers in various parts of the District of Columbia and nearby Maryland areas. The cost of transporting such programming off post is borne by the organization receiving the program.

### MISSION AND PROSPECTS

To quote Dr. Paul W. Schafer, Executive Director of the WRAMC Television Division: "All who have training and education responsibilities are concerned with a continuing shortage of qualified teachers. There are just not enough to go around, this being no less true in medicine than in the field of education generally. Simple quantitative approaches to this problem have not reduced our continuing deficiency. It appears that something new, something qualitatively different is needed. The Television Division of Walter Reed Army Medical Center is dedicated to the thorough exploration of the training and educational potential of our most powerful means of audio visual communication—color television."

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### EMOTION AND GILSIONS

"Not only functional disorders but also gross organic lesions in the gastrointestinal tract can be caused by emotional stimuli. The functional disorders include nervous vomiting, anorexia nervosa, nervous diarrhea, constipation, and irritable colon. The disturbances of function may lead to the organic lesions of which good examples are peptic ulcer and chronic ulcerative colitis. Such problem cases require study and treatment of the total organism and may necessitate consultation between social service department, psychiatrist, and internist."

—LOWELL D. SNORF, M.D.

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# HERNIA OF MORGAGNI ASSOCIATED WITH HIATAL HERNIA

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**H**ERNIA through the foramen of Morgagni is a relatively uncommon condition, slightly more than 100 cases having been reported in the literature. Harrington<sup>1</sup> encountered only 4 cases in a series of 270 diaphragmatic hernias of various types. The combination of an esophageal hiatal hernia with a hernia of Morgagni must be rare. To our knowledge the only reported case is the one presented by Harrington<sup>2</sup> in 1941, however, the retrosternal hernia did not contain colon, only omentum being present. Our recent experience with a case of esophageal hiatal hernia combined with a Morgagni hernia that contained colon prompted this report. Furthermore, during the past few months we have encountered two additional cases of simple Morgagni hernia, and these will be summarized briefly.

## CASE REPORTS

**Case 1.** A 62 year-old woman had been seen in the clinic at this hospital for four months prior to admission on 9 September 1957. There were multiple complaints and an element of hypochondriasis was first suspected. The patient's chief symptoms were dizziness, retrosternal and epigastric distress especially after meals, nausea, infrequent vomiting, chronic cough occasionally productive of small amounts of yellow sputum, and intermittent pain over the tip of the left scapula. She also complained of chronic constipation requiring laxatives every 3 or 4 days. She had lost about 23 lbs during the nine months prior to admission. Her past history was noncontributory.

The physical examination was essentially negative except for the presence of a mid line surgical scar with some diastasis recti abdominis. Routine laboratory studies, an electrocardiogram, and a gallbladder series were within normal limits. A roentgenogram of the chest in the posteroanterior projection showed elevation of the diaphragm on the right and a large mass at the right cardiophrenic angle (fig. 1). The gastrointestinal series, utilizing the Valsalva maneuver and Trendelenburg position, demonstrated a large esophageal hiatal hernia. A barium enema demonstrated a loop of transverse colon entering the chest by way of the right retrosternal space (figs. 2 and 3).



*Figure 1 (case 1) Roentgenogram showing elevation of the diaphragm on the right and a large mass at the right cardiophrenic angle.*

A diagnosis of Morgagni hernia with concomitant esophageal hiatal hernia was made and an operation was performed on 12 September. Through a high left paramedian incision a hernia of Morgagni containing a 20-cm loop of transverse colon and a sliding hiatal hernia with a 6- by 6- by 8-cm gastric pouch were found. The two hernias were easily reduced and repaired and the postoperative course was entirely uneventful. The patient was discharged on 21 September with complete relief of her symptoms.

**C 2.** A 28-year-old man was admitted to this hospital on 27 May 1957 with a diagnosis of infiltration of the middle lobe of the right lung. The patient was essentially asymptomatic and the infiltrative lesion in the right lung field at the cardiophrenic angle had been discovered on routine roentgenographic examination of the chest.

Physical examination and routine laboratory studies on admission were essentially negative. Roentgenograms of the chest revealed a



*Figure 2 (case 1) Barium enema demonstrating a loop of transverse colon entering the chest by way of the right retrosternal space*

semispherical density contiguous with the right cardiac border and measuring 8- by 5-cm in diameter (fig. 4). Fluoroscopy revealed that the mass did not pulsate. Inspiratory and expiratory films of the chest showed some change in size and configuration of the mass. A barium enema failed to demonstrate colon above the diaphragm. Bronchoscopy, blood volume measurements, pulmonary function tests, and an electrocardiogram were within normal limits.

On 28 June a right thoracotomy was performed and a hernia through the foramen of Morgagni was encountered. There was an 8- by 4 cm mass of omentum in the hernial sac but it did not contain colon. The mass was reduced into the abdomen and the defect repaired with interrupted silk sutures. The patient's postoperative convalescence was uneventful and he was discharged to full duty on 17 July.





*Fig. 3 (case 1) Gastrointestinal series (tilt with Valsalva maneuver and Trendelenburg position) demonstrating sigmoidal hiatal hernia, abdominal meniscus below M. pectus, with loop of colon in right costal space.*

C. 3. An 18-year-old man was admitted to this hospital on 19 July 1957 with a history of a productive cough. He had experienced an episode of shortness of breath while lying in bed which he described as an obstruction in the lower chest that seemed to restrict his breathing. He also had noted substernal and epigastric distress not related to food intake. His past history was noncontributory.

Physical examination revealed a young white man in no acute distress. Routine laboratory studies were within normal limits. A roentgenogram of the chest in the posteroanterior diameter revealed a mass at the right cardiophrenic angle. Lateral chest films demonstrated a retrosternal mass about 4 by 3 cm in size (figs. 5 and 6). A barium enema was negative.



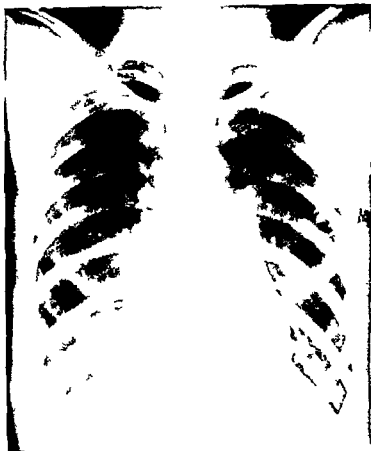
*Figure 4 (case 2) Posteroanterior roentgenogram showing semi-spherical density contiguous with the right cardiac border*

On 29 August a right thoracotomy was performed and a small hernia of Morgagni about 4 by 3 cm in diameter and containing only omentum was found. The defect was easily repaired with several interrupted silk sutures. Postoperative convalescence was uneventful and the patient was discharged on 13 September with no complaints.

#### DISCUSSION

The foramen of Morgagni is a triangular defect located in the anteromedian portion of the diaphragm. It is bounded by the posterior surface of the sternum and the sternal and costal diaphragmatic attachments. The space contains fatty areolar tissue and affords passage to the superior epigastric arteries. Hernia through the foramen is variously called Morgagni hernia, subcostosternal hernia, parasternal hernia, retrosternal hernia, retrocostoxiphoid hernia, and hernia through Larrey's spaces.

Morgagni hernias are considered to be the least common of all the diaphragmatic hernias. Basically they are of the direct type.



*Figure 5 (case 3) Posteroanterior roentgenogram showing mass at the right costophrenic angle*

and contain a peritoneal sac. They generally are considered to be embryologic in origin, although the majority of cases reported have been noted in patients over 40 years of age. Presumably obesity and increasing intra-abdominal pressures function as precipitating factors. These hernias occur mainly on the right side, the left retrosternal space apparently being strengthened by the pericardium.

The symptoms are variable and range from minimum to rather severe, largely depending on what organ is included in the hernia. The most common organs involved are colon and omentum; infrequently stomach, small intestine, or liver may be found. Strangulation may occur but seems to be uncommon. Abdominal symptoms include indigestion, epigastric pain, eructations, nausea, vomiting, dysphagia, and chronic constipation. Gastrointestinal bleeding or signs of intestinal obstruction may be present.

Symptoms in the chest may result from compression of the lung, producing dyspnea, chronic cough, and hemoptysis. Interference



*Figure 6 (case 3) Lateral roentgenogram showing retrosternal mass just above the diaphragm.*

with normal cardiovascular function may cause shoulder pain, substernal pain, palpitations and even cyanosis. The symptoms usually are aggravated by exertion or by assuming a supine position shortly after eating, and not uncommonly are relieved by vomiting.

The diagnosis of Morgagni hernia seldom is difficult if one is aware of this condition. Symptoms may simulate disease of any intra abdominal organ or of the cardiorespiratory system. Routine roentgenographic examination of the chest usually will reveal a rounded cardiophrenic angle density that in lateral views is seen to be located retrosternally. This would suggest any one of a number of lesions, such as pericardial cyst, lipoma, teratoma, neoplasm of the lung, bronchial cyst, lymphoma, and encapsulated pleural fluid, but if colon is present in the hernia at the time

of the examination haustrations may be seen or some type of intestinal pattern may suggest itself. A gastrointestinal series utilizing the Trendelenburg position and the Valsalva maneuver may be helpful. A barium enema frequently will show colon located in the retrosternal space. Even if only omentum is present in the hernia one may get the impression from a barium enema that the colon is being pulled cephalad. Induction of pneumoperitoneum and pneumothorax may be useful in diagnosis, in some cases.

The treatment of Morgagni hernia is surgical. It is generally believed that the transabdominal approach is superior to the thoracic approach. Not infrequently however, a positive diagnosis can not be made preoperatively. In these cases thoracotomy is mandatory. the transthoracic approach usually posing no difficulty in repair of the defect. After the hernia is reduced, the excess portion of the sac is excised and small defects simply repaired with interrupted sutures overlapping the edges of the diaphragm. In large hernia the anterior margin of the defect may be sutured to the anterior chest wall or to the posterior rectus sheath. Fascial grafts or sutures have been used for repair as have the round ligament and transversalis fascia.

### SUMMARY

Three cases of hernia of Morgagni have recently been treated surgically at this hospital. In one of these cases there was an associated esophageal hiatal hernia. Such a combination must be extremely rare, only one case having been found in the literature. This case presented many symptoms all of which were completely relieved by surgical intervention.

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# COMPLICATIONS OF MECKEL'S DIVERTICULUM

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**I**T is the purpose of this article to describe the complications encountered in 41 cases in which Meckel's diverticulum was found during surgical procedures at this hospital in the 42 month period from January 1954 through June 1957

Meckel's diverticulum the commonest of a number of recognized abnormalities of the vitelline duct results from incomplete obliteration of the duct, which in early fetal life connects the yolk sac with the intestine. Arising from the antimesenteric border of the ileum usually less than 1 meter from the ileocecal valve Meckel's diverticulum is said to occur in about 2 per cent of the population.<sup>1</sup> A definite familial incidence of this anomaly has been documented.<sup>2</sup> In one case in the present series, the patient's father earlier had required resection of such a diverticulum.

A diverticulum may be easily identified by its separate blood supply the prominent omphalomesenteric vessels, which arise from the intestinal arcade and pass over the bowel out along the wall of the diverticulum to its tip. These vessels occasionally persist at their usual location in the absence of a grossly demonstrable diverticulum. Usually lined by intestinal mucosa diverticula not uncommonly contain gastric, duodenal pancreatic or colonic tissue, alone or in combination.

In our patients the diverticula varied from 1 to 20 cm in length and the largest was 3 cm in diameter. They were located from 20 to 90 cm from the ileocecal valve.

## COMPLICATIONS

A variety of complications may arise from this anomaly most of the commoner ones being observed in the present series. When a fibrous remnant persists from the tip of the diverticulum to the umbilicus a loop of intestine may become obstructed around it.

The structure if attached only at its base may invert and form the leading point of an ileal intussusception Torsion obstruction and gangrene of the entire structure can occur The most frequently observed complications however are related to the presence of heterotopic tissue notably gastric mucosa This by the action of acid and pepsin forms a peptic ulcer in a portion of the diverticulum lined by intestinal mucosa or in the nearby ileum with hemorrhage perforation or acute ulcerative diverticulitis

Granulomas and neoplasms benign and malignant are reported Nearly half of all patients with complications develop symptoms in infancy or early childhood More than two thirds of all diverticula as estimated from autopsy series do not cause any symptoms or complications

Of the 20 patients in our series in whom the primary disease was directly related to a Meckel's diverticulum 14 had simple diverticulitis 1 had volvulus with perforation 2 presented in intussusception with acute ulceration of the intussuscepting diverticulum and 3 had uncomplicated volvulus without diverticulitis Among the 17 cases of diverticulitis there were 8 instances of ulceration Of these 4 were perforated and in the other 4 there was a history of clinically significant bleeding

In the total of 41 patients 5 diverticula were not resected because of an acute surgical condition requiring treatment elsewhere in the abdomen Gastric mucosa present in 38.8 per cent of the 36 resected diverticula was found in 10 (58.8 per cent) of the 17 cases with diverticulitis including all 8 cases with ulceration which either had bled or perforated

### CLINICAL FINDINGS

Five patients in whom Meckel's diverticulum was the site of pathologic lesions gave histories of prior gastrointestinal symptoms Two complained of recurring nausea vomiting and abdominal pain for a year One 11 month old infant had repeated rectal bleeding over a three and one half month period A seven year old child with a perforated ulcer in a diverticulum had had several bloody stools six weeks earlier One patient with a small perforation gave a six month history of intermittent right sided abdominal pain

The only constant symptom in all patients with acute illness related to Meckel's diverticulum was abdominal pain the location and character of which varied with the nature of the lesion The most usual physical finding was right lower quadrant abdominal tenderness leading in eight cases to a preoperative diagnosis of acute appendicitis In five cases the diagnosis of Meckel's

diverticulitis was made preoperatively, in four the preoperative diagnosis was intestinal obstruction due to postoperative adhesions, and volvulus, intussusception, and perforated viscus were each diagnosed once

Laboratory examinations were of little aid in diagnosis. White blood cell counts ranged from 8,600 to 15,400 cells per  $\mu$ l. The lowest concentration of hemoglobin, 4 grams per 100 ml, occurred in a 4 month old infant bleeding from an ulcerated diverticulum. Meckel's diverticulum was not demonstrated radiographically in any of our patients prior to operation.

Nine of our 41 patients had previous intra abdominal operations, and 5 of these 9 were in the group of patients who developed complications related to their Meckel's diverticula. Appendectomy had been performed previously in four. One 38 year old patient had undergone three previous laparotomies including an appendectomy, a unilateral salpingo oophorectomy and removal of the other ovary and tube. At the time of her fourth operation she was found to have a volvulus of the small bowel and omentum about a Meckel's diverticulum 15 cm in length with its tip adherent in the pelvis. Another patient with volvulus of small bowel about a band from a diverticulum had undergone laparotomy for a gunshot wound of the abdomen six years previously.

### TREATMENT

Treatment of Meckel's diverticulum at this hospital during the three and one half year period varied with different surgeons. Of the 41 diverticula encountered 5, as noted previously, were not resected. The remaining 36 were treated as follows: oblique resection of diverticulum 14, longitudinal resection of diverticulum 7, transverse resection of diverticulum 6, transverse resection of diverticulum including wedge of ileum 5, resection of a short segment of ileum including diverticulum with end to-end ileoileostomy 3, and resection of terminal ileum (containing diverticulum) and right colectomy for lymphosarcoma of cecum 1. Two of the short ileal resections were made necessary by the presence of gangrenous bowel incident to ileal intussusception. The third such resection was performed electively, and this case was of special interest because of subsequent anastomotic complication, the only such problem in the series. Of the 5 diverticula not excised, 4 were incidental findings. The fifth occurred in a patient who was convalescent from cervical laminectomy. He was moribund at the time of laparotomy, which was performed urgently for peritonitis caused by perforation of the cecum. The perforation had resulted from volvulus about a band leading from the abdominal wall to a noninflamed Meckel's diverticulum. Treatment consisted of lysis of the obstructing



band and exteriorization of the cecum. The death of this patient from sepsis constituted the single mortality of the series.

### SURGICAL COMPLICATIONS

Apart from the postoperative death which resulted from delayed diagnosis of volvulus of the cecum progressing to perforation before laparotomy the only major complication was that of stenosis of the anastomotic site after a limited resection of ileum. This patient was originally explored after a period of observation during which time he had complained of vomiting and severe abdominal pain and no gross intraperitoneal pathologic condition was discovered. Appendectomy was performed and a large Meckel's diverticulum was excised incidentally. Postoperatively there was persistent paralytic ileus with fever and a changing pattern of bizarre neurologic findings. The diagnosis of Guillain Barre' syndrome was considered. On the 14th postoperative day gastrointestinal motility returned with evidence of mechanical small bowel obstruction. Re exploration revealed stenosis at the site of previous anastomosis. After resection of the stenotic segment and re establishment of intestinal continuity the postoperative course was uncomplicated and the patient later returned to full active service. The one other instance of partial obstruction responded promptly to intestinal decompression and did not recur.

Four wound infections all occurred in cases of incidental diverticulectomy, three in association with appendectomy and one with lysis of adhesions for intestinal obstruction. Secondary paralytic ileus (three cases) responded in each instance to conservative measures.

### DISCUSSION

The potential complications of Meckel's diverticulum have been known for more than 50 years and our experience is not materially different from that of others who have written on this subject.<sup>1-7</sup> Intussusception due to invaginated Meckel's diverticulum in infants is not rare and one of our cases occurred in a seven month old infant. In adults intussusception occurs less frequently and Ponka<sup>8</sup> stated that these patients often give a long history of recurring bouts of periumbilical pain as in our other case of intussusception occurring in a 26 year-old man. Volvulus of bowel caused by a band between diverticulum and the abdominal wall occurs infrequently and our finding only two cases in a three and one half year period confirms this observation.

The one death in this series resulted from a volvulus that went unrecognized beyond the time when successful treatment could have been instituted. The presence of gastric mucosa in these diverticula increases the danger of complications. The

finding of gastric mucosa in 38.8 per cent of our patients is a somewhat lower incidence than is reported in series comprised entirely of children most of whom have been operated on for primary pathologic conditions in the diverticula. As adults enter the series increasing numbers of incidentally excised, asymptomatic diverticula will dilute this percentage toward the figure of 20 per cent reported by Jav and associates<sup>8</sup> for specimens found incidentally at laparotomy.

All of our eight patients with ulceration four with perforation and four with hemorrhage were in the group showing gastric mucosa. In connection with this finding Berran, Schneider and Pot s<sup>11</sup> believed that bleeding or rupture occur only when gastric mucosa is present. In none of our eight patients was ulceration found on the opposite ileal wall as was found in patients of Smith and Woodward.<sup>12</sup> No pancreatic tissue was found in any of the diverticula of our series and one noninflamed diverticulum was found to be lined entirely by normal colonic mucosa.

Five complications occurred in patients who had previously undergone one or more laparotomies suggesting that a more careful search for Meckel's diverticulum needs to be made at the time of every abdominal procedure. In five other patients a noninflamed diverticulum was found but not removed because of an acute pathologic condition elsewhere in the abdomen. Jav and associates<sup>8</sup> state that in view of the fact that one in five of the specimens found incidentally at laparotomy contain gastric mucosa, all Meckel's diverticula should be removed on discovery. We would agree with the more conservative view of Baker and Marshall<sup>9</sup> who believed that when a diverticulum is encountered in the course of an unrelated abdominal procedure all other contingencies must be evaluated before excision of the diverticulum is added to the hazard of other intra-abdominal surgery. The presence of a narrow neck or of an adhesive band to the umbilicus is generally considered to be a strong indication for removal whereas generalized acute inflammatory disease, a prolonged primary procedure or the necessity of intestinal resection tend to contraindicate incidental diverticulectomy.

#### SUMMARY

Of 41 patients with Meckel's diverticulum treated at this hospital over a three and one-half year period, 20 had complications such as intussusception, volvulus or diverticulitis; the latter being associated with ulceration, bleeding, and perforation. In eight patients with bleeding, ulceration and perforation gastric mucosa was present in the diverticula.

Oblique resection of the diverticulum at its base is preferred when the adjacent ileum is normal although occasionally seg-

mental resection of ileum and end-to-end ileal anastomosis is necessary. Serious complications due to Meckel's diverticulum occur with sufficient frequency to warrant removal of all diverticula when found incidentally provided all other factors are evaluated before diverticulectomy is added to other intra-abdominal procedures.

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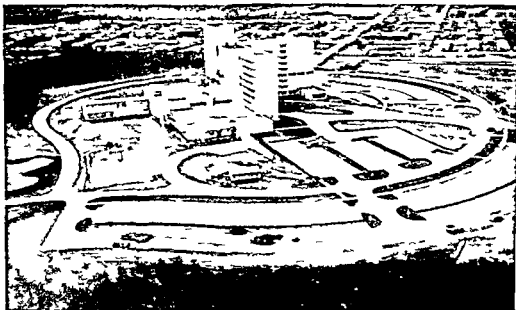
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### EDUCATION UNENDING THE HERITAGE OF MEDICINE

DAN C. OGLE *Major General USAF (MC)*

**A** GAIN it is my privilege and an honor to address the civilian and military citizens of this community, as a representative of the United States Air Force and its medical service.

In contemplating the patriotic history of this area, I feel humble to stand on such ground, yet I am proud to have the opportunity of formally introducing this hospital to this community and to the great profession of military medicine and to dedicate its service to our country. The Air Force is fortunate in being so well established and so well received as it is here.



*New U. S. Air Force Hospital Lackland Air Force Base, Tex.*

Few communities can boast of the brilliant patriotic history that so endears Texas and San Antonio to the hearts of the American people. For 250 years this community has been a center of military and cultural development. Under various flags it has

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Presented at the dedication ceremonies of the new hospital, Lackland Air Force Base, Tex., 16 November 1957.

General Ogle is Surgeon General, United States Air Force.

always been America though not until 1845 did it come under the Stars and Stripes. For over one hundred years the Alamo served as a center of religion, teaching, refuge, and inspiration. Then on 6 March 1836 it became one of the outstanding inspirational shrines of American history and patriotism.

Much also can be said of the Cathedral of San Fernando standing at the exact center of the 36 square miles of the city. Other missions, schools, cathedrals, and fortresses have contributed greatly to the picturesque and inspiring history of this State. This land and its many patriots are endeared to all the people of the United States as well as to you of Texas. It is known the world around that no one loves his native land more than a Texan. That is good. Theodore Roosevelt is said to have remarked that the man who loves other countries as much as his own stands on a level with the man who loves other women as much as he loves his own wife.

It would take a long time to recount the history of the military installations of San Antonio. However, I would like to speak of military medical education in this area.

The School of Aviation Medicine was moved to Brooks Field on 30 June 1926. With its growth requirements soon developed for more space and for more diverse professional activities. As a consequence, the School was moved into new quarters at Randolph Field on 30 October 1931. A new headquarters building for the School of Aviation Medicine was dedicated in April of 1943. Earlier this year, on 10 May, I had the honor of participating in ground breaking ceremonies for another new School of Aviation Medicine which is now being constructed at Brooks.

I wish to call your attention also to the Army Medical Field Service School at Fort Sam Houston and to Brooke Army Hospital which has been an outstanding treatment and teaching center for years. I wish to express official thanks to the Army for the many opportunities afforded members of the Air Force Medical Service attending special courses at that school and Brooke Hospital which enable them to better serve their country in medical activities. There are bonds of understanding in the fields of medicine that allow productive interservice cooperation. The installations I have mentioned together with the many other regional military hospitals and special clinical and laboratory activities have stamped this geographical area as a significant center of military medicine.

## NEED FOR MEDICAL EDUCATION

I have spoken of the military, cultural and medical teaching activities of this area as a means of introducing a theme for further discussion—a theme of medical education. This new hospital that we dedicate today is a great teaching hospital.

In addition to providing first class medical care for the military community, this hospital will be utilized for years to come as one of the principal teaching institutions for medical officers and health specialists who serve the Air Force.

The growth of the great body of medical knowledge and the requirement for higher levels of medical education and detailed knowledge in so many clinical specialties make it necessary that physicians and others engaged in the health sciences be given frequent and stimulating opportunities to improve their knowledge and their skills. They need the teaching atmosphere of institutions such as this, as well as experience in hospital practice to provide the intellectual stimulation necessary for continual acquisition of new knowledge and understanding for no physician's education is ever completed. Stagnation here like stagnant water breeds the vectors of health failure.

It is our ambition in the Air Force that our community hospitals scattered throughout the world each become in some measure an educational institution in which medical officers will have an opportunity of practicing their profession, and where they will enjoy an interchange of ideas between themselves and civilian specialist consultants of the community in which they are located. Only by such means can we maintain the high standards of medical care deserved by those in uniform and only through continual education and training can we be assured of being professionally prepared for the exacting demand of national defense.

Perhaps you have heard military men speak of education and training. These two terms are names of related programs. Training is the development or the perfection of skills and technics while education is the acquisition of new knowledge. We must not consider education and training solely from the standpoint of that which is prescribed for academic recognition but rather as that which fits us for progressive and productive service. It is true that we need the tools of knowledge and procedures if we would continue to build during the years following medical school. However, what we need more than the sheepskins of graduation and specialist certification is the desire and the ability to contribute effectively throughout a lifetime of progressive service. We continue to increase in stature as physicians or specialists in health fields with the growth of our fund

of knowledge in science and technology only if this knowledge is translated into service and the practice of good medicine. There is a compelling need for the desire to grow during our productive years—the desire to know more and to contribute more just for the personal satisfaction of positive accomplishment as distinct from mere recognition of academic attainment.

And what is the genesis of this need to know more and do better on our part? Fundamentally it is our awareness that there are men, women and children who need the best of medical care—and in the military service it is even more—it is the need of engineers who must create weapons and munitions operable within the limits of human tolerance—it is the need of men who must survive the strange environments of modern combat—it is the need of our country which cannot long endure unless each citizen becomes fully worthy of his hire.

Doctor Detlev W. Bronk, president of the National Academy of Sciences, in a recent article in *Air Force* on the education and use of scientific manpower said: "If we are going to utilize our scientific manpower better, we must somehow revive the realization in our population that there is a joy and a zest in hard work. Our Nation became great because men had things they wanted to do with devotion. Unless we can recapture that love of hard work, we will utilize our manpower badly."

He was not preaching drudgery or such devotion to duty that enjoyable, wholesome recreations are missed. Hard work should never be allowed to shut out the tempering and sustaining qualities of recreation or a sense of humor. In contemplating the idea of hard work, I ran across an anonymous quotation which may express the experience of many of us: "I have met but few people in my time who were enthusiastic about hard work, and it was just my luck that all of them happened to be men I was working for at the time."

#### ART VS SCIENCE OF MEDICINE

In the practice of medicine today, the physician needs more help than he recognized the need of twenty years ago. So many of the obtuse complaints, illnesses and injuries that the doctor sees in his office today point up his personal and his office limitations in arriving at a satisfactory diagnosis or a course of treatment. He is limited in the evaluation of his therapy unless highly technical laboratory assistance is available to perform essential tests. A working knowledge of the complicated biochemistry of sugar, albumen, globulin, the conjugated proteins, cholesterol, sodium, potassium, calcium and all of the large family of steroids, hormones, vitamins and enzymes has become a necessity for today's sophisticated practice of medicine. Not

only does the clinician recognize this need but an increasingly educated public demands more scientific medical attention than that furnished by the triad of the Empirics. But let me hasten to add that this triad of chance observation, preceptorship, and comparative analogy has supported medicine for more than two thousand years and probably still accounts for much more medical care available to the civilized world than does the science of ivory towers and I would be the last to advocate that this art of medicine be discredited.

I do advocate however that it is the duty of all men and women in health fields to become more knowledgeable in the science of medicine and health maintenance because good health good nutrition good living conditions, and good minds provide the greatest resources of this country and the greatest hope for world peace.

In contemplating peace there seems to be a relationship between war and disease. War is a form of politico-economic social disease which, like the maladies of the flesh, can be avoided by continuous health precautions. Our ambitions and methods of attaining victory over disease are very much like our ambitions to attain victory over war itself. Such victories however cannot be attained by wish fulfillment but only by a constructive alliance between men of good will whose faith and trust in themselves their country and their God stimulate them to work and wisdom instead of inactivity, futility, or complacency.

Medical science has attained many victories over diseases. We seldom see smallpox typhoid yellow jack plague or typhus. We are reducing the incidence of polio and influenza tuberculosis is gradually coming under control soon we may be able to say the same thing of cancer heart disease arthritis and many of the others but it can never be said of these diseases that they have been conquered except by great expenditures of money time effort education dedication and tireless work. Like war itself the diseases we have apparently conquered are lying dormant ever ready to strike back at a relaxed or careless world that neglects attention to the continuing tasks of control.

There is a need for all physicians whether they be in the military service or in civilian life to be in frequent contact with a teaching atmosphere. Experience is a great teacher but the science of medicine is too large for one man's experience to keep him at the peak of professional competence. The mutually teaching atmosphere of hospitals such as this must be distributed as best we can to all our hospitals both large and small. This is easier in the military services because our operational policies provide that physicians move about at various intervals throughout their military life. Our career control management disallows that a man



responsible for clinical care of patients stagnate in some circumscribed area out of contact with the progressive stimulation of continuing medical education

The needs of medical education that I have discussed here are in the minds of medical educators everywhere The American Medical Association's Council on Medical Education and Hospitals briefly defines postgraduate medical education as those educational activities engaged in by persons possessing the degree of Doctor of Medicine which are primarily designed to keep them abreast of their own particular field in medicine These activities concern basic medical education as well as new developments in the field

### MEDICAL SCHOOL IN SAN ANTONIO

This community of San Antonio is a growing center of clinical and military medical education The Brooke Army Hospital the Army Medical Field Service School the Air Force School of Aviation Medicine this teaching hospital here at Lackland and the growing clinical capacity of your medical societies and hospitals all point in this direction

During the process of selecting a site for the new School of Aviation Medicine a heavily weighted factor served to keep San Antonio from a position of unquestioned first choice We believed and still believe that our new School and research laboratories should be in the neighborhood of a first-class medical school that much could be gained by association between two such teaching and research institutions There was no medical school here but San Antonio was finally selected because of many overriding advantages and because we had faith that this city would one day have its own medical school I hope it will come in the near future It is a community and national need that should not be denied

Today I have discussed the future of this hospital in terms of its leavening influence in the fields of continuing medical education and training for the Air Force Medical Service To that end and to the primary mission of furnishing a high level medical and hospital service to the military community this new Lackland Air Force Hospital is hereby dedicated

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# AVIATION PATHOLOGY

## The Role of the Pathologist in Investigating Aircraft Accident Fatalities

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THE primary purpose of this article is to review the sequence of events in the progress of aviation pathology and to indicate the role therein of the Armed Forces Institute of Pathology (AFIP). This newly created discipline was launched in March 1955 by a conference held at the Institute, the objectives of which have been reported by Berry.<sup>1</sup> The conference, which was attended by aviation representatives of the Armed Forces of the United States, Canada, and the United Kingdom, was called to explore ways and means of counteracting the mounting toll of aircraft accident fatalities in the countries represented.

Aviation is confronted with many complex developments affecting both men and machines. As a result, new problems have arisen and old ones have been brought into sharper focus. Among the foremost is that of flight safety. Though much progress has been made in achieving greater safety, with a resulting decline in the overall accident rate per number of flying hours, yet the total number of fatalities has increased. Thousands of lives are lost each year, including those of hundreds of rated pilots. The human suffering cannot be measured, and economic losses are staggering. Reporters, quoting authorities, have proclaimed that accidents cost the Navy and Air Force some two million dollars a day in material losses alone. The appalling loss of highly trained men and expensive machines stems from our rapid technological advances, with the creation and employment of high performance aircraft capable of attaining speeds and altitudes once considered fantastic. And the end is not yet in sight, as space itself is being challenged.

By reason of this high total of aircraft accidents, and particularly those of unexplained origin, which number 14 per cent and contribute 40 per cent of the fatal accidents,<sup>2</sup> a concerted effort was initiated to investigate more thoroughly the role of the human element. This step is justified by reports that well over

50 per cent of accidents are attributed to pilot failure.<sup>3</sup> The primary objective for the investigation of aircraft accidents is to determine the cause and thereby prevent recurrence. Over the years engineers and material specialists have demonstrated the value of a detailed examination of the fragments of a wrecked aircraft in their search for clues to the disaster. Less attention had been given to a careful study of the human remains aimed at determining if structural failure of the man may have contributed to the cause of the accident.

Eventually it became apparent that one field of medical science had not been fully utilized by the aircraft-accident investigation team. That field is pathology. The contribution that the pathologist could make was dramatically demonstrated in the investigation of the British *Comet* disasters over the Mediterranean in 1954. The investigating pathologists discovered from autopsies performed on bodies recovered that the occupants had suffered a violent upward and forward motion as revealed by head and chest injuries and skin abrasions. It was deduced that the injuries were due to sudden decompression of the cabin pressure from a structural defect in the overhead toward which the occupants appeared to have been forced. The latent energy in a large pressurized cabin such as the *Comet's* flying at a cruising height of 30 000 ft. has been calculated as being equivalent to that contained in 100 pounds of high explosive. Later the reconstruction of wreckage recovered from one of the planes and the testing of others proved that the deduction of the pathologists was correct inasmuch as a 162 sq ft defect was discovered located over a seam above one of the windows. With this and other data as a background the need for intensive study of the pathology of aircraft accident fatalities was recognized.

### JCAP ESTABLISHED

In November 1955, acting on recommendations of medical officials who had attended the March conference at the AFIP, the Department of Defense issued a directive establishing the Joint Committee on Aviation Pathology (JCAP). This committee is now composed of representatives from the U S Army, Navy, and Air Force, the Royal Canadian Air Force, and the Royal Navy and Air Force. The Directive designated the Armed Forces Institute of Pathology as the central co-ordinating facility for investigation of the pathology of aircraft accident fatalities. To meet this responsibility the AFIP organized a Forensic and Aviation Pathology Section by integrating an Aviation Pathology Unit within the already existing section on Forensic Pathology. This was a natural merger inasmuch as forensic pathology is the subspecialty that has long been engaged in the medical investigation of accidental violent and unexplained deaths. An Aviation Toxicology Laboratory also was set up solely for the support of this program.

## SCIENTIFIC CONFERENCE HELD

In November 1956 the JCAP sponsored a second conference, again held at the AFIP. There were about 80 military and civilian participants, including representatives from the United Kingdom and Canada. In addition to pathologists and flight surgeons, engineers and other individuals concerned with flight safety also were present. Twenty four scientific papers were read at this meeting and a résumé of the proceedings is now available from the AFIP as JCAP Memorandum No. 3. Since then several more papers on this subject have been presented at scientific meetings, and a few articles<sup>4-7</sup> dealing with the functions of pathology as they relate to aviation medicine and flight safety have appeared in the literature. Each of the armed services has issued regulations and instructions concerning the pathologic support of aircraft accident investigations. These are listed in Appendix 1 by number and title, together with a brief summary of each.

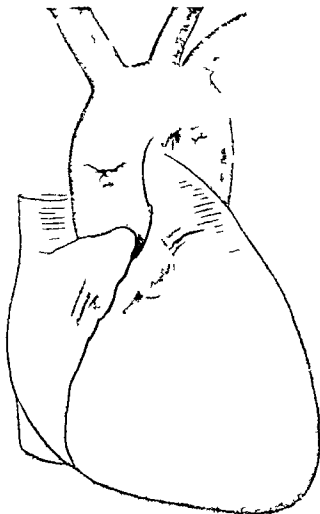
## THE PATHOLOGIST AND HIS SERVICES

The Armed Forces have progressed rapidly in developing the new field of aviation pathology and in utilizing the knowledge and experience of their existing group of trained pathologists in aircraft accident investigations. In the military services, the significant role of the pathologist in this area of aviation medicine is not only recognized but has become established. To be contributory, however, the work of the pathologist must encompass more than the time honored, routine procedures of pathology. Some degree of special training and an acute awareness of the many factors involved in the "man-aircraft" relationship is necessary. The combination of pilot, flight surgeon, and trained pathologist in one individual is ideal, and the military services are fortunate indeed to have a small nucleus of such highly qualified specialists who are assigned to aviation pathology.

At the AFIP, the Aviation Pathology Section is currently staffed by four Air Force pathologists, one of whom is a qualified pilot, and in the near future this group will be augmented by a Navy pathologist. The Aviation Toxicology Laboratory is staffed by a trained toxicologist and three technical assistants.

Specialized training in aviation pathology at the AFIP covers not only the processing of pathologic material received from aircraft fatalities and interpretation of the findings but also field trips for active participation in the investigation of selected aircraft accidents. The Commander, Headquarters Command, Bolling Air Force Base, Washington, D. C., has made air transportation available to the AFIP on an on call basis as required in the implementation of this program. Participation in a few such field investigations has already been accomplished, the latest being that concerned with the Pan American Airline disaster in the

of pulmonary embolism Intravascular fat can be found within the alveolar walls in well over 90 per cent of the aircraft accident cases minimal in about a third of the cases but in marked degree



arw

Figure 1 Sketch of the aorta and most at right most probable site of rupture caused by abrupt deceleration.

in 2, per cent Comparable findings have been reported in battle casualties Other pulmonary emboli following injury are those consisting of bone marrow in approximately 20 per cent of cases Liver (fig 4) brain (fig 5) and air emboli also may be seen occasionally in the pulmonary vessels The observation of these emboli tends to vary directly with the avidity with which one searches for them

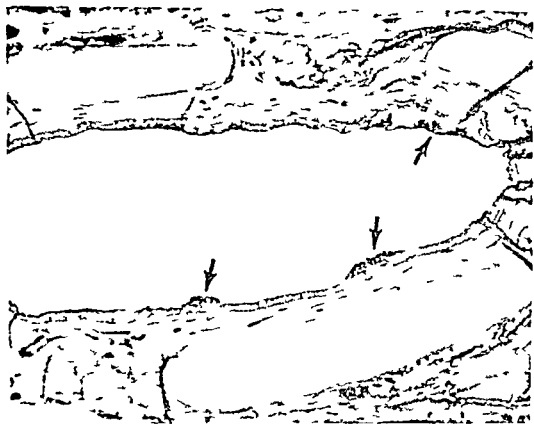


Figure 2 Photomicrograph showing soot particles on the tracheal mucosa. These are indicative of inhalation of smoke (Hematoxylin and eosin stain,  $\times 13$ )

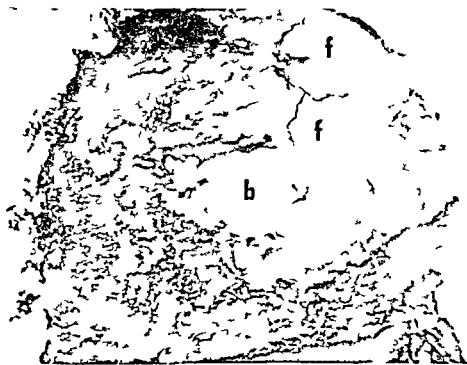


Figure 3 Photograph of skull following burns showing the stellate fractures (f) and extrusion of cerebral tissue (b) caused by heat.

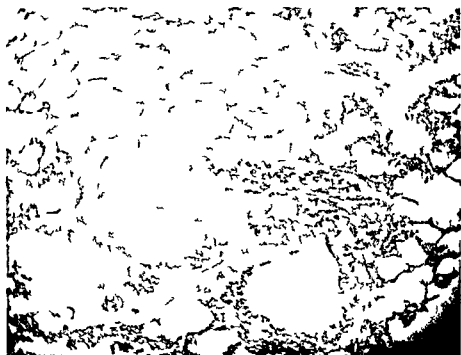


Figure 4. Photomicrograph of lung showing emboli from liver situated at the bifurcation of a pulmonary vessel (Hematoxylin and eosin stain  $\times 65$ )

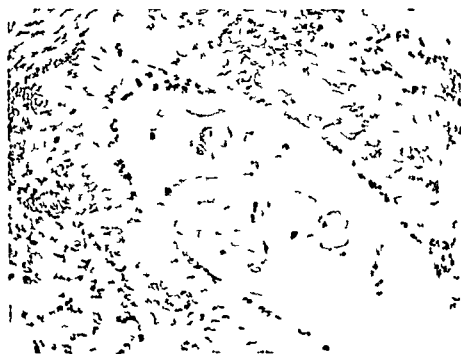


Figure 5. Photomicrograph demonstrating numerous miliary bacterial emboli in a pulmonary vessel (Hematoxylin and eosin stain  $\times 160$ )

### Pre-existing Disease

In the realm of pre existing disease, the presence of coronary sclerosis offers much room for speculation. A coronary attack in the pilot of a single place aircraft could well result in another unexplained aircraft accident. Although many of the coronary arteries examined in deceased pilots show moderate to marked coronary sclerosis, the following three cases illustrate the problem the pathologist faces in evaluating coronary arteries from autopsy material, and the necessity for a cautious interpretation of the significance of the findings.

*Case 1* A 40-year-old pilot was conducting strafing and bombing missions upon surface ships. During one of these attacks his aircraft was seen to "nose-up" then return to its horizontal flight path and finally dive into the side of the ship. Examination of the wreckage showed no evidence of mechanical failure. The autopsy revealed advanced coronary arteriosclerosis with an acute thrombosis causing sudden incapacitation of the pilot resulting in the accident.

*Case 2* A 37 year old pilot had made normal radio contacts and was flying as scheduled. When he failed to make his next routine radio check an immediate search was instituted. The fatally injured pilot and wreckage were found three days later. Although numerous injuries were present the heart showed severe coronary arteriosclerosis and in addition there was myocardial fibrosis that indicated previous episodes of coronary insufficiency. In this case the question can be raised "Was the accident the result of a coronary attack?"

*Case 3* A 27 year old pilot of an F 102 aircraft was killed in an engine failure accident. Radio communications immediately prior to the accident revealed he was physically and mentally alert. There had been no previous history of cardiac symptomatology though the autopsy showed severe coronary arteriosclerosis. In this case there was no evidence to indicate that coronary disease had played any role in the accident however if the fact of engine failure had not been known pilot failure through coronary insufficiency might well have been incriminated as the cause.

It is well known that coronary artery arteriosclerosis is not confined to the elderly or middle aged. This was clearly demonstrated by AFIP pathologists in a wound ballistics study in the Korean Conflict, when they examined the coronary vessels of 300 young American soldiers with average age of 22.1 years who were killed in action. Their report<sup>11</sup> indicated that 77.3 per cent of these casualties, showed some gross evidence of coronary arteriosclerosis, in all degrees from "fibrous" thickening to large atheromatous plaques causing complete occlusion of one or more major vessels.

Some of the examples in the AFIP files of pre existing disease which produced sudden disabling episodes or death in pilots,



include brain tumors sickle cell anemia laryngocele and abdominal adhesions

From a study of 62 cases of colloid cysts of the brain on file at the AFIP three cysts were found to have killed or incapacitated aviators<sup>1</sup> In these cases any marked exertion which would be expected to increase cerebral blood flow and therefore the brain volume would in all probability result in a narrowing of the third ventricle around the cyst thus favoring a blockage of fluid flow with resulting symptoms of headache vomiting et cetera These symptoms may begin and cease abruptly Gravity forces in flight causing increased intracranial blood volume would presumably be effective in initiating this condition

In persons with sickle cell anemia or the sickle cell trait splenic infarction or sickle cell crisis initiated by hypoxia may occur during air travel<sup>12</sup>

It thus is seen that even though aviators are given rigid physical examinations periodically and are under the almost constant surveillance of qualified flight surgeons "pre-existing disease" still may remain undetected and create an ever-present hazard in flight operations The demonstration of telltale pathologic lesions by the pathologist has accounted for a number of otherwise unexplainable accidents If the day comes when the clinician is equipped to diagnose some of these disease conditions now demonstrable only by the pathologist some of the hazards now inherent in man's control of the air will be overcome

### RESEARCH IN AVIATION PATHOLOGY

In addition to the part played by the AFIP in the more or less routine work noted above research in aviation pathology is being actively carried on While some of this research is in support of Navy and Air Force investigative projects at various research centers much of it is primary investigation performed within the Institute itself

One such support study involved the gross and microscopic pathologic evaluation of rats explosively decompressed to 65 000 feet This research project was performed at the Air Crew Equipment Laboratory Naval Air Materiel Center U S Naval Base Philadelphia Pa and was supported from the standpoint of pathology by the AFIP In an altitude chamber rats were explosively decompressed from sea level pressure to a simulated altitude of 65 000 feet, and total fixation in Formalin was performed in that environment The detailed pathologic findings in these animals is the subject of a report by Gell Hall and Mostofi

Despite over 100 abstracts of varying merit in the literature this was the first time that a study of the effects of pure explosive decompression had ever been accomplished Pathologic

studies in the past had not been performed until recompression had intervened. Recompression could have erased the major pathologic findings demonstrated in this project, such as extensive emphysema of the thoracic wall, air bubbles in major blood vessels, and displacement of the upper abdominal viscera into the lower thorax.

Another cooperative study in which the AFIP rendered support was a joint Navy Air Force project on the effects of prolonged G forces, performed at the Naval Aero Medical Acceleration Laboratory, Johnsville, Pa. In these experiments, chimpanzees were subjected to centrifugal G forces exerted by the Johnsville human centrifuge.

Subjected to a centrifugal force of 40 G for 60 seconds while placed in various positions, none of the animals showed an irreversible pathologic abnormality, although in all cases the traumatic force resulted in varying degrees of hemorrhage. Some animals were unconscious when removed from the centrifuge (having been in a fully reactive state prior to the test), but within 24 hours they appeared normal clinically. When sacrificed 24 to 48 hours later, the autopsy findings consisted only of varying degrees of hemorrhage, mostly within the pulmonary parenchyma and limited mainly to those areas located most peripherally to the lines of the test force. In those animals facing away from the center of the centrifuge, large areas of hemorrhage were found, particularly within the distal portions of the extremities and the periorbital tissues, as a direct result of the pooling of blood caused by the centrifugal forces.

Other research projects dealing with aviation problems in which the AFIP has given support have centered chiefly around the problems of cosmic radiation and the effects of rapid acceleration and abrupt deceleration. One of the more revealing projects of the acceleration series was that of sudden exposure to supersonic wind blast, such as would be experienced by ejection from high performance aircraft. The Air Force, employing the "snort" track at the U S Naval Ordnance Test Station, China Lake, Calif., subjected two chimpanzees to rapid acceleration with a relatively slow deceleration component. The accelerations were in the neighborhood of about MACH 1.8 and within a period of 12 seconds the animals attained that speed from a dead stop. In both instances, the flight suit was ripped from the animal. The anteriorly exposed skin surfaces of the body were compressed and desiccated, producing a tanned, leathery appearance (fig. 6). There was elevation and denudation of the superficial epidermis from the effects of the wind blast and generated heat.

Cosmic ray studies have been carried on in association with the Aero Medical Field Laboratory, Holloman Air Force Base, N. Mex. Balloons, carrying mice in sealed capsules, have been

sent to cruise the stratosphere in order to determine the biological effects of cosmic rays upon living mammals <sup>1</sup>



Figure 6. Photograph of desiccated compressed k from a teno exposed surface of the chmpa x (left) contrasted with o alte d ki from posterior exposed surface (right) Not the pilation, the de iccat d and had d pid rm s a d the comp e s d d m

Research conducted primarily at the AFIP has been chiefly within the environmental problem area. Studies are now under way to correlate the lactic acid concentrations associated with hypoxia with possible structural changes within the cell. Improved methods for the post-mortem detection of acute hypoxia are being sought, and currently the AFIP laboratory is evaluating the significance of a rise in urinary pH in hypoxic states. If this latter proves useful it would certainly be a more easily performed test for hypoxia.

The Aviation Toxicology Laboratory is devoting considerable effort to methodology for the determination of small therapeutic amounts of drugs present in tissues of aircraft accident fatalities. Customarily the toxicologist deals with lethal amounts of drugs usually in relatively large quantities but the current problem facing aviation pathologists is the detection of minute amounts of drugs for the most part taken without medical advice. Iontophoresis has proved a satisfactory method for initial detection of such drugs as the tranquilizers, antihistamines, barbiturates, alkaloids, and those taken for the prevention of motion sickness.

The JCAP with the support of the AFIP is endeavoring to bring about the indoctrination of (1) flight safety personnel in the need for careful observation and reporting of near accidents, (2) aircraft accident investigating teams in the need for pathologic support, (3) commanding officers in facilitating performance of autopsies, (4) pathologists in careful post-mortem examination and correlation of the findings with the aircraft and safety equipment, and (5) medical examiners, coroners, and pathologists throughout the United States, Canada, and the United Kingdom on the need for detailed pathologic investigation of aircrew fatalities.

## CONCLUSIONS

While much benefit has accrued from the current method of pathologic study, there is no substitute for adequate and accurate "on the spot" post-mortem examination. Pathologists trained for such investigations of selected aircraft accidents would be ideal. A beginning has been made, and eventually this may be possible on a wider scale. By such means, it is believed that both military and civilian flight safety programs could benefit immeasurably. The staggering economic losses might well be lessened and the toll in human lives be drastically reduced.

## SUMMARY

High performance aircraft have accounted for an increase in the number of accidents caused by so-called pilot error, and accidents of undetermined cause have increased to 14 per cent (40 per cent of the fatal accidents). In order to evaluate properly the pilot-plane combination, it is necessary that in all aircraft accidents an intensive medical investigation be instituted. In an attempt to fulfill the requirement for a complete medical investigation, the Joint Committee on Aviation Pathology (JCAP), with representatives from the United Kingdom, Canada, and the United States, was established. The Armed Forces Institute of Pathology (AFIP) was designated as the central co-ordinating laboratory for JCAP, and organized a new section on Aviation Pathology, staffed by four pathologists and other supporting personnel.

The AFIP has authorized direct shipment of tissues to the Institute for examination. Instructions for the collection and shipment of specimens have been promulgated. The importance of on the spot investigation by the pathologist is recognized, and in selected aircraft accidents support will be provided by the AFIP. An aircraft accident fatality is studied from three main viewpoints: (1) environmental conditions, (2) traumatic factors, and (3) pre-existing disease. It is important that a complete examination, including all these facets be made. Research activities sponsored or supported by the AFIP have included studies on explosive decompression, effects of centrifugal G forces, effects of rapid acceleration and abrupt deceleration, morphologic changes in acute hypoxia, and methods for detection of therapeutic amounts of drugs in post-mortem tissues.

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## APPENDIX

## J i t A l F A m y N y

*Med cal Service Joint Committee on Aviation Pathology* AFR 160-127  
AR 15 97 BUMED INST 6510 6 3 September 1957 This regulation pre-  
scribes the organization functions and membership of the Joint Com-  
mittee on Aviation Pathology

## A l F

*Medical Service Medical Investigation of Aircraft Accident Fatal-  
ities* AFR 160-109 12 October 1956 This regulation requires that a  
medical officer conduct or instigate a thorough medical inquiry con-  
cerning the cause and nature of fatal injuries sustained in aircraft acci-  
dents The investigation will include the performance of autopsies

*Aircraft Accident Autopsy Report* AF Form 500 15 October 1956  
This form is used in conjunction with AFR 160-109 and serves as a  
guide for autopsies on aircraft accident fatalities

*Medical Service—Performing Postmortem Examination.* AFR 160-35  
Section G Paragraph 37 27 June 1956 This regulation states that an  
autopsy should be performed when death occurs while the person was  
serving as an aircraft crew member in a military aircraft

*Flying Safety—Aircraft Accidents* AFR 62 14 25 January 1956 This  
regulation defines terminology establishes responsibility and pre-

scribes procedures for investigating and reporting Air Force aircraft accidents and incidents

*Aircraft Accident—Prevention Investigation Reporting* AFM 62 5, 1 February 1956 This regulation outlines in detail the procedures to be followed in accident investigation and reporting including the medical aspects

#### **Navy**

*Manual of the Medical Department U S Navy* Article 17 24 Post Mortem Examinations and Autopsies This instruction states that the medical officer should make every effort to obtain autopsies on aircrew fatalities

*Navy Aircraft Accident Incident and Forced Landing Reporting Procedure* OPNAV INST 3750 6B 20 May 1956 This instruction sets forth procedures establishes control promulgates disposition and establishes responsibilities in regard to Navy aircraft accidents incidents and forced landings In addition it requires that medical officers make every effort to obtain autopsies on aircrew fatalities

*Aviation Pathology Program* BUMED INST 6510 6 3 September 1957 This instruction summarizes the Navy's role in support of the triservice aviation pathology program

#### **Army**

*Accident Reporting* SR 385 10-40 Change 7 24 June 1957 This regulation outlines Army procedure for aircraft accident investigation

*U S Army Aircraft Accident Investigation* TB AVN 8 31 August 1956 This regulation outlines in detail accident investigation and reporting including the medical aspects

# MALPRACTICE AND THE SERVICE DOCTOR

RAYMOND COWARD L. t e t C I t JAGC USA

**M**ALPRACTICE and professional liability are matters of direct concern to every member of the medical profession whether he is engaged in private practice or is a doctor serving in the Armed Forces. At common law there was no duty on the part of the doctor to render medical care to an ill person and the law in this country imposes no liability on the doctor for refusing to take a case but once medical care is undertaken by the doctor he becomes responsible for his acts. This is true even if the patient is a charity case.

Recognizing that he should practice his profession with the welfare of the patient uppermost in mind, the doctor asks how he can do this and still protect himself against malpractice claims. Are these two concepts incompatible? How is the service doctor affected by malpractice claims as compared to the private practitioner? Should a medical officer carry malpractice insurance? Are there definite steps that can be taken or procedures which may be followed by either a private or service doctor that will furnish substantial protection to him and either reduce the likelihood of malpractice claims or avoid them altogether?

The realization that these and related questions are constantly in the minds of doctors has prompted the writing of this article in an effort to help the individual doctor and particularly the medical officer to arrive at sound conclusions with respect to this complicated medico-legal field. Some of the principles discussed are applicable not only to the medical officer but also under certain circumstances to the service dentist, nurse or other member of the medical team after making allowance for the different standards of education, training, experience and knowledge applicable to the different professions.

## DEFINITIONS

What is malpractice? It has been defined as "Any professional misconduct, unreasonable lack of skill or fidelity in professional or fiduciary duties, evil practice or illegal or immoral conduct." More specifically, as applied to physicians and surgeons, it means bad, wrong, or injudicious treatment of a patient profes-

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sionally, and in respect to the particular disease or injury, resulting in injury, unnecessary suffering, or death to the patient, and proceeding from ignorance, carelessness, want of proper professional skill, disregard of established rules or principles, neglect, or a malicious or criminal intent.<sup>2</sup>

The term *malpractice* appears to be used more and more by the courts as though synonymous with *negligence* on the part of the physician, surgeon, dentist, or nurse. Negligence is "The omission to do something which a reasonable man, guided by those ordinary considerations which ordinarily regulate human affairs, would do, or the doing of something which a reasonable and prudent man would not do."<sup>3</sup>

In general a legal action based on negligence (malpractice) is founded on a tort as distinguished from an action on a contract as a result of an agreement between the parties concerned. However, the action may be based on a contract in an instance where the doctor agreed to cure or to make a specified improvement in the patient's condition and failed to do so as a result of his medical treatment.

A tort is defined as "A wrong independent of contract. A violation of a duty imposed by general law or otherwise upon all persons occupying the relation to each other which is involved in a given transaction."<sup>4</sup> Three elements of every tort action are existence of a legal duty from defendant to plaintiff, breach of duty, and damage as approximate result.<sup>5</sup>

### RES IPSA LOQUITUR

With respect to negligence cases there is a doctrine in the law known as "*res ipsa loquitur*" or "the thing speaks for itself." In malpractice proceedings, plaintiffs and their attorneys often encounter difficulty in obtaining the services of experts in the medical and nursing professions to testify that a colleague was negligent. The doctrine of *res ipsa loquitur* is of great assistance to the plaintiff under such circumstances. Except for this doctrine how could plaintiffs otherwise prove that paralysis, burns, foreign substances in the abdomen, and other such conditions were the result of negligent acts?

Three conditions are necessary for the rule of *res ipsa loquitur* to apply: (1) The accident is of a kind that does not occur in the absence of *someone's negligence*; (2) the injury is caused by an instrumentality within the *exclusive control of the defendant*; and (3) the accident is of a kind that the *plaintiff could not have contributed to by his conduct*. How this doctrine is applied depends on the law of the particular state. In some states proof of the three required conditions is considered as circumstantial evidence and negligence may be inferred. In other states proof of these three conditions creates a presumption of negligence and



places the burden on the defendant to overcome the presumption. A *presumption* is a deduction which the law requires the trier of facts to make an *inference* being a deduction which the trier may or may not make according to his own conclusions, a *presumption* is mandatory an *inference* permissible.

A leading case in the United States on the doctrine of *res ipsa loquitur* as applied to malpractice suits is that of *Ybarra v Spangard*.<sup>7</sup> The essential facts in this case are

Plaintiff entered a private hospital for an appendectomy to be performed by the defendant. On the day of the operation he was wheeled into the operating room by a nurse who was an employee of Dr. Swift who owned the hospital. The anesthetist also an employee of Dr. Swift adjusted plaintiff for operation pulling his body to the head of the operating table and laying him back against two hard objects at the top of his shoulders about an inch below his neck. The anesthetic was administered and plaintiff lost consciousness. He awoke next morning in his room attended by two nurses also employees of Dr. Swift.

Plaintiff testified that prior to the operation he never had had any pain or injury to his right arm and shoulder but that when he awakened he felt a sharp pain between the neck and the point of the right shoulder. He received diathermy treatments but the condition spread to the lower part of his arm. He could not lift or rotate his arm and developed paralysis and atrophy of the muscles round his shoulder.

Plaintiff instituted proceedings against the physician who diagnosed the case, the owner of the hospital, the surgeon, the anesthetist and the three nurses. After his testimony attorneys for the defendants asked that the suit be dismissed on the ground that the plaintiff did not prove any defendant to be negligent and indeed by all legal standards he did not. But the plaintiff contended that his testimony showed the existence of the three conditions necessary to invoke the doctrine of *res ipsa loquitur* that the inference of negligence was established and that the plaintiff should prevail.

The defendants claimed the doctrine did not apply in this case that the condition that the instrumentality was in the exclusive control of defendant did not exist and that the doctrine cannot apply where several defendants are involved and there is a division of responsibility. The court decided for the plaintiff and said

But we do not believe that either the number or relationship of the defendants alone determines whether the doctrine of *res ipsa loquitur* applies. Every defendant in whose custody the plaintiff was placed for any period was bound to exercise ordinary care to see that no unnecessary harm came to him and each would be liable for failure in this regard. Any defendant who negligently injured him and any defendant charged with his care who so neglected him as to allow injury to occur would be liable. The defendant employers would be liable for the neglect of their employees and the doctor in charge of the operation

would be liable for the negligence of those who became his temporary servants for the purpose of assisting in the operation

"We do not at this time undertake to state the extent to which the reasoning of this case may be applied to other situations in which the doctrine of *res ipsa loquitur* is invoked. We merely hold that where a plaintiff receives unusual injuries while unconscious and in the course of medical treatment, all those defendants who had any control over his body or the instrumentalities which might have caused the injuries may properly be called upon to meet the inference of negligence by giving an explanation of their conduct."

This case shows the importance of keeping careful, complete, and accurate case histories and records on each patient. This is important not only for the civilian doctor or nurse but for the service doctor or nurse as well. The doctrine of *res ipsa loquitur* is at issue in a large proportion of malpractice cases in litigation and is frequently held applicable to individual cases by the courts.

### RESPONDEAT SUPERIOR

The rule of law known as "respondeat superior" or "let the master answer" has applicability in malpractice cases in certain instances. This rule provides that an employer or principal is liable for the torts committed by an employee or agent in the course of employment or action as an agent. The rule does not absolve the employee from liability; rather, it permits the injured party to sue both the employee and the employer. Frequently the employer is in a better financial position and consequently the suit is brought against the employer or jointly against the employee and employer so that the injured party has a better chance of recovering damages for his injuries.

### FEDERAL TORT CLAIMS ACT

It is a general rule of law that a government may not be sued without its consent. This is based on the theory of sovereign immunity and can be traced back to the common law in early English history. It was said "The King can do no wrong," and consequently no one was permitted to sue the Crown.

However, the Federal Tort Claims Act<sup>1</sup> (FTCA) was passed by Congress and became effective in the United States in 1946. Prior to this, the United States could not be sued for negligent acts of its employees or agents. This Act created consent of liability on the part of the Federal Government where claims are established for damage to or loss of property, or for personal injury or death caused by negligent or wrongful act or omission of any employee of the Government while acting within the scope of employment or office in circumstances in which the United States, if a private person, would be liable to a claimant in accordance

with the law of the place in which the act or the omission occurred.

The FTCA provides specifically that the acceptance by a claimant of an award or a settlement shall constitute a complete release by the claimant of any claim against the United States and against the employee of the Government whose act or omission gave rise to the claim. The FTCA *excludes* any claim for negligence arising out of the exercise of a discretionary function relating to policy or interpretation, miscarriage of mails, assessment or collection of custom duty, quarantine, assault and battery, false imprisonment, false arrest, malicious prosecution, abuse of process, libel, slander, misrepresentation, deceit, interference with contract rights, the operations of the Treasury, or combat activities of military forces during time of war. It also excludes any claim for negligence arising in a foreign country or in the operation of the Tennessee Valley Authority or the Panama Canal.

In effect the FTCA establishes consent on the part of the Federal Government to liability under the rule of *respondeat superior* for negligence of employees committed in the course of employment. There is no consent to being sued for claims arising under the exemptions stated. A person having a claim for any cause other than negligence as limited would be in the same position as were claimants sustaining negligent injuries prior to the enactment of the FTCA and as are claimants who have sustained injuries committed by state governmental employees. Such claimants cannot institute legal proceedings in courts; they are required to seek the aid of Congress in case of a claim against the Federal Government or the aid of the appropriate state legislature in the case of a claim against a state government for the enactment of a special law to compensate them for damages sustained.

The United States District Courts have exclusive jurisdiction over suits brought under the FTCA, however, claims under \$1,000 may be compromised and settled by the heads of federal agencies and departments. The Army has published regulations setting forth the procedure for settling these claims. Claims over \$1,000 may be compromised and settled but must be approved by a Federal Court. Claims not settled may be determined by proceedings in court which must be commenced within a specified period of time depending on the statute of limitations in effect where the cause of action arose and generally within one year from the date of the commission or omission constituting negligence.

Also, certain claimants may file an administrative claim but not a suit under the provisions of the Military Claims Act of 1943.<sup>2</sup> This statute has been implemented by regulations of the Army.<sup>1</sup> Thus a claimant may have a remedy under one of the two

above named Acts. He may also bring an action against the individual doctor, but he is more likely to bring the action against both the doctor and the United States.

If an Army or other Government agency doctor is sued individually, he may request that the case be removed to a Federal District Court if the action is brought in a state court.<sup>12</sup> In any case where an Army doctor is sued individually or sued jointly with the United States, a report of litigation, in accordance with published regulations, should be submitted to the Department of the Army.<sup>13</sup> Arrangements may then be made by the Office of The Judge Advocate General with the Department of Justice for the local United States Attorney to make an appearance in the case and defend the doctor and the United States.

If a judgment should be obtained against an Army doctor individually, the Department of the Army would, in all probability, sponsor a private bill in Congress to give him relief. *In the past it has not been necessary to seek such legislation, as no case has been reported where an Army doctor has been held by a decision of a court to be individually liable*, although bills are now pending before Congress to give relief to two Army employees held individually liable in traffic cases. If a judgment is obtained against the United States, subsequent recovery from the individual doctor is barred by the statute.<sup>14</sup>

A major difficulty in applying the rule of *respondeat superior* is in determining whether the employee was acting within the scope of his employment; however, "scope of employment" has been defined to mean "acting in the line of duty" when applied to a member of the military forces.<sup>15</sup> The Federal Government therefore is liable for the acts of its employees in the same manner as a private employer is liable.

A case as to whether the employee was acting within the scope of his employment was decided in *Hatt v U S*,<sup>16</sup> wherein it was held that the Government was not responsible for the negligent operation of a government truck by a sergeant of the National Guard, because the man's job description did not provide for his driving military vehicles and consequently he was acting outside the scope of his employment. In another case, *Dishman, v U S*,<sup>17</sup> an employee of the Veterans Administration, had carbolic acid poured into his ear for an ear pimple by a physician of the Veterans Administration. The Court held the Government was liable, as the regulation of the Veterans Administration authorized treatment of minor ailments of employees and the physician was therefore acting within the scope of his employment.

The United States would not be liable, even if the physician was acting within the scope of his employment, if the cause of action falls within one of the specific exemptions to the Federal

Tort Claims Act. One of the exceptions for example is an action based on assault and battery. This tort is the basis for many professional liability suits such as those involving unauthorized operations and treatments. In the case of *Moos v U S*<sup>18</sup> which arose in Minnesota the plaintiff's right leg and hip were operated on in a Veterans Hospital when it was his left leg and hip that needed the operation. His suit was dismissed as being an action for assault and battery and not actionable under the FTCA. It should be kept in mind, however, that the plaintiff could still sue the individual doctor in a case such as this.

Another type of case excluded under the FTCA is any claim for negligence arising out of the exercise of a discretionary function relating to policy or interpretation. Problems in this area have arisen in the past with respect to furnishing medical care to dependents of military personnel. The question of what is or is not a discretionary function has caused the courts considerable difficulty. It was held in *Denny v U S*<sup>19</sup> that since admitting dependents of military personnel to government hospitals is discretionary, no action could be brought for negligence under the FTCA. However, it was held in *Grigalauskas v U S*<sup>20</sup> a Massachusetts case that once the discretion is exercised and the patient admitted, the discretionary function ceases and the Government is liable for any subsequent negligent acts. It also was held in *Costley v U S*<sup>21</sup> that the use of an anesthetic containing a harmful substance was not a discretionary act and did not fall within the discretionary exception under the FTCA. After the Texas City disaster it was held in *Dalehite v U S*<sup>22</sup> that action against the United States under the FTCA could not be maintained because of the principle of discretionary function. Recent decisions of the Supreme Court in the case of *Indian Towing Co v U S* and in the *Eastern Airlines case* indicate that the discretionary act exclusion is now limited to those decisions made on a policy making or planning level and decisions made on an operational level could not be used as a basis for denying a cause of action under FTCA even though some discretion is involved.

The question of whether a serviceman has a right to sue under the FTCA was settled in *Feres v U S*<sup>23</sup>. The opinion covered three cases. One *Jefferson v U S*<sup>24</sup> was a suit by a veteran who had a towel left in his abdomen during an operation in an Army hospital while he was still on active duty. Another case was *Griggs v U S*<sup>25</sup> which concerned an officer in the Army who died after treatment in an Army hospital while the *Feres* case involved an officer of the Army who died in a fire in the barracks. The Court held that none of these claims could be maintained under the FTCA because the injured parties were servicemen on duty at the time of injury or death. The opinion

points out that the Government has financially provided for members of the Armed Forces in different ways and that traditionally members of the armed services could not sue the Government for injuries received while on duty. It would bring chaos to the order and discipline of the Armed Forces to allow every service man to sue the Government for every real or fancied wrong he might suffer.

The limitations discussed with respect to discretionary functions would apply also to civilian employees of the Government. Prior to 1949 it appears that a civilian employee could elect to proceed under the FTCA or the Federal Employees' Compensation Act.<sup>22</sup> In 1949 Congress amended the latter Act so as to make it the exclusive means of compensation for a civilian employee killed or injured "while in the performance of his duty."<sup>23</sup> It will be noted, however, that in the case of *Dishman v. U.S.*<sup>24</sup> the Court held that an employee of the Veterans Administration could bring an action under FTCA for negligence of a physician of the Veterans Administration in treating a pimple in the ear, as the injury was not incurred in the performance of duty and therefore was not governed by the Federal Employees' Compensation Act. Very few cases are found which involve claims under the FTCA by civilian employees against government physicians. This indicates either that such claims are being handled under the Federal Employees' Compensation Act or that comparatively few civilian employees are being treated by government physicians.

The question may be raised as to whether the enactment by Congress of the Dependents' Medical Care Act<sup>25</sup> is likely to result in more malpractice claims against service doctors. Section 103 (a) of the Act provides:

Whenever requested medical care shall be given dependents of members of a uniformed service, and dependents of persons who died while a member of a uniformed service, in medical facilities of the uniformed services subject to the availability of space, facilities and the capabilities of the medical staff. Any determination made by the medical officer or contract surgeon in charge, or his designee as to availability of space, facilities, and the capabilities of the medical staff shall be conclusive. The medical care of such dependents provided for in medical facilities of the uniformed services shall in no way interfere with the primary mission of those facilities.

This statute has codified a substantial part of what was in the law and pertinent regulations prior to its enactment. In addition to setting out the types of medical care that may be furnished it specifically prohibits or limits others which formerly were prohibited or limited by policy and regulation, such as ambulance service, domiciliary care, and treatment of nervous and mental

of the helicopter rigged to pickup baskets engagement with a sling attached to the basket was possible. A rapid pickup by a hovering helicopter resulted (fig 1)

To assure a proper sequence of arrival and thereby avoid confusion and loss of time at the unloading site it was mandatory that serialization of the supplies and equipment be made. The tents, poles, camouflage nets and tools necessary for tent erection were contained in the 13 initial cargo loads. Subsequent loads contained the equipment of each hospital section. Following the arrival of this equipment the initial supply block organic to the company was transported. The last heli lifted items of cargo were the C rations. These were taken in place of B rations and the galley, thus additional weight was diminished. In this manner observing a priority arrangement in debarkation a predicted arrival of supplies and equipment was achieved. A total of 53 external loads were required. Because of its delicacy and the possibility of damage the roentgen ray tube assembly apparatus was the only internal load. By using exclusively this external means of cargo transport it was possible to pick up a loaded heli basket in less than one and one half minutes and unhook one in a matter seconds.

Augmentation and replenishment of medical supplies using helicopters was one of the major aims of the exercise. The resupply for the collecting and clearing company came from the Medical Supply Section of the Medical Battalion. In the exercise this section was embarked aboard ship. Since amphibious supplies were prepared in predetermined assemblies as is standard practice it was not unduly difficult to modify these assemblies into appropriately sized loads so they could be fitted in heli baskets. These were serialized so that in any given basket it was known just what items were present. Serialization also allowed any component part of the resupply to be sent independently had it been desired. Twelve heli baskets were required to accommodate these supplies. Anesthesia gases, intravenous fluids, drugs, splints, litters, blankets et cetera were all resupplied successfully by this means.

One last innovation was necessary for the exercise. To provide realism for training purposes and so that some basis would exist for requesting a resupply of medical material supplies had to be utilized however the expenditure of costly medical items was unjustified. This problem was resolved by establishing storage areas marked used medical supplies in each medical facility.

As each simulated casualty was treated, the actual supplies which normally would have been expended were placed in the provided storage area without opening or unwrapping. These constructively expended supplies were not used again during that phase of the exercise. Using this innovation the "expenditure" of medical supplies to provide realism and test resupply was accomplished without needless wastage of medical material.

Having satisfied the pre exercise requirements of organizing and training the involved units, as well as having attempted to make appropriate modifications where possible in personnel employment, equipment, and supplies that portion of the exercise to be discussed below was begun.

#### CHRONOLOGY OF THE EXERCISE

Units of the Third Medical Battalion were embarked aboard the U S S *Tulare* (AKA 112) a cargo ship having a heli deck. On the day of the exercise the ship was anchored approximately 2,000 yards offshore. At the first light of dawn on 26 May 1957 personnel and equipment of "D" Company the collecting and clearing company utilized in this phase of the exercise were debarked from the U S S *Tulare* by helicopter. The time required for movement of the personnel was 23 minutes. Upon being landed ashore at a preselected site erection of the hospital was begun (fig 2). This company became fully established and camouflaged and was ready to process casualties in less than three hours. The ship-to shore movement was accomplished using 11 helicopters (HMR(C) 162 and HMR(L) 163). Personnel, basic equipment and organic supplies including the initial supply block, were transported ashore. The movement of cargo required 1 hour 45 minutes.









*Figure 6 The sorting station aboard ship*

similar way supplies were "expended." Once treatment had been rendered the patient was placed at bed rest. Hospital charts were maintained, and the patients were even fed in bed.

Casualty reporting was another aspect of this operation which was highly stressed. Because the aim of this article is primarily directed toward the medical aspects of this phase of the exercise further mention will not be made except to note that innovations were utilized and tested.

The exercise did not cease until several hours after nightfall so that a test of night operations could be made. During the exercise a total of 234 "casualties" were heli lifted and a total of over 46 000 pounds of cargo were carried by helicopter.

#### DISCUSSION

Military commanders have long recognized that superiority in battle can be achieved through rapid movement of their personnel, equipment, and supplies.<sup>7</sup> Greater dispersion of forces as is dictated by nuclear warfare has increased the demand for mobility of combat elements. Not only must the combat troops have this capability, but it is mandatory that medical supporting units likewise possess the ability to be displaced readily and rapidly. In triphibious warfare desired mobility for medical elements can

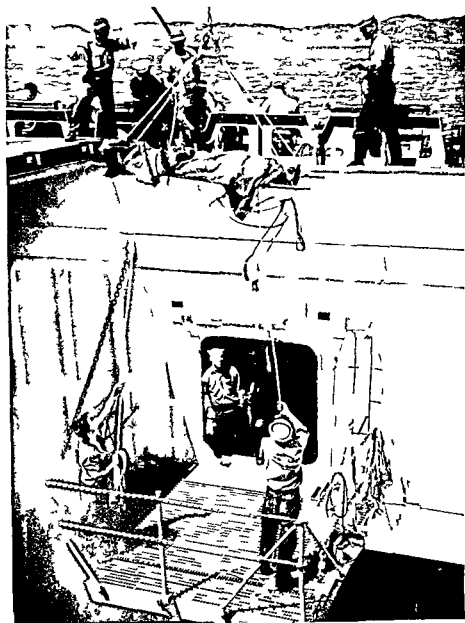


Figure 7 Lifting a casualty from the deck to the deck of the battle damage station

be achieved by using helicopters. As a result medical units with the Marine Corps have been using and developing new techniques to adapt themselves to the capability afforded by the helicopter. During the Korean Conflict the Marine Corps used helicopters extensively for casualty evacuation. The Army Medical Department also has utilized helicopter support for casualty

evacuation.<sup>1</sup> In triphibious operations, however, casualty evacuation is but one aspect of the medical aid that must be rendered. The portion of the exercise discussed in this article presents some of the other aspects.

This article is believed to be one of the first reporting a major field exercise of such magnitude having a primary objective of medical techniques to be used in casualty management. Although there are frequent maneuvers and field operations in which medical companies, and at times an entire medical battalion participate, the prime aim of such exercises is tactical. This field problem then was indeed unique. Moreover, it is believed that this is the first medical exercise reported in which an attempt was made to simulate treatment realistically, process casualties and their reports, evacuate selected individuals as far as the seaward echelon, and there continue the play of the problem aboard ship, thus exercising all levels of medical support. That such an exercise was of inestimable value cannot be contested, and that new knowledge was gained can be conceded. Some of the modifications made in the equipment of the medical company cannot be considered original for they have been advocated previously by others.<sup>1, 2</sup> The realistic utilization of these and other modifications and innovations set forth in this article were developed for this exercise by the joint efforts of Navy and Marine Corps personnel of the Third Marine Division, the First Marine Air Wing, and the Amphibious Group Western Pacific, working together toward the common goal of enhancing the effectiveness of medical support for those who in the future may be engaged in amphibious battles.

#### SUMMARY

In this article an attempt has been made to present some of the medicomilitary features of a recently conducted field medical exercise. Prior to the exercise, classroom training was given to marines who served as simulated casualties. Modifications were made in personnel, organization, equipment, and preparation of supplies so that greater mobility would be achieved and helicopter movement made possible. Innovations were introduced in the use of medical supplies. Helicopter transported emergency medical teams were organized and equipped to provide emergency care for a large number of casualties suddenly introduced into the exercise. Transportation by helicopter and establishment of a medical company clearing section, sending supplies to the company by helicopters, realistically processing simulated casualties through the company, seaward evacuation of "casualties" by helicopters, and subsequent treatment aboard ship were accomplished. The details have been described with the aim of providing data of interest to help others in planning similar future exercises.

and with the hope of stimulating further needed modifications for amphibious medical support.

### CONCLUSION

To ensure that medical care will be adequate to keep pace with changing concepts of amphibious warfare additional exercises of like character and a continuing revision of the organization and equipment of the existing medical units with the Fleet Marine Force are necessary. Future planning should be directed toward the goal of creating a complete self contained medical unit capable of rendering definitive care and able to be transported by helicopter.

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### CURLING'S ULCER

Evidence of gastrointestinal (usually duodenal) ulceration was seen in 20 out of 1 000 patients hospitalized for burns over a period of 78 months. The ulceration was found at autopsy in 17 of the 80 patients who died; it was accepted as the immediate cause of death in 4. The concentration of pepsin in the urine was higher in the patients with the more severe burns and this was associated with high concentrations of pepsin and hydrochloric acid in the gastric juice.

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GERARD F. LANCHANTIN, 1 Lt. MSC USA  
CURTIS P. ARTZ, Lt. Col. MC USA  
*in Journal of the American Medical Association*  
p 141 May 11 1957



## Clinicopathologic Conference

U S Naval Hospital, Oakland Calif \*

### CHEST PAIN

**Summary of Clinical History** A 46 year old man was admitted to this hospital for the second time on 20 July 1955 complaining of severe, oppressive anterior chest pain of short duration, and with a history of edema of the legs, dyspnea, and orthopnea of one month s duration

The final illness dates back four years, at which time the patient experienced his first episode of transient wheezing, dyspnea, and hemoptysis, with a recurrence nine months later, for which he was hospitalized here At that time he was found to have left heart enlargement, hepatomegaly and pulmonary congestion Despite a 12 hour episode of left upper quadrant pain, myocardial infarction could not be unequivocally diagnosed Electrocardiograms showed frequent ectopic beats and inversion of the T wave in leads I, V<sub>1</sub>, and V<sub>6</sub>

Following discharge, the patient remained in good health until several months before his present admission when he began to develop effort angina and exertional dyspnea Outpatient department records describe the appearance of a grade II apical systolic murmur and electrocardiographic demonstration of a right bundle branch block In the month prior to admission, his symptoms increased and edema of the legs developed

Past history included flu in 1917 tonsillectomy and adenoidectomy in 1932 pleurisy in 1939 and chronic alcoholism in the past. There was no history of acute rheumatic fever The patient retired six years ago, not because of physical disability

R r Adm John Q Ow l y MC, USN Comm nding Officer From the Medical Service  
C pt. R bert O Canada MC USN Ch f

**Physical Examination** On admission the patient looked both chronically and acutely ill and his skin was ashen with both pallor and cyanosis. His pulse was rapid and regular except for frequent premature contractions. Blood pressure was 110/60 mm Hg. Examination of the chest revealed wheezing and crepitant rales were present in both bases. The heart was described as greatly enlarged with a grade II precordial systolic murmur; a gallop rhythm was noted. There was massive edema of the legs. No evidence of thrombophlebitis was noted on admission. The remainder of the physical examination was not remarkable.

**Laboratory Studies** Complete blood cell counts and urinalysis were normal. Blood urea nitrogen was 22 mg per 100 ml. Roentgenograms and electrocardiograms are presented in the discussion.

**Course in Hospital** The patient was initially treated for his congestive heart failure with a low sodium diet, digitalis, quinine, morphine, oxygen, and diuretics. Despite this therapy he continued to manifest more congestive failure with recurrent bouts of shock, hemoptysis, fever to 103 F, and rapid pulse with frequent premature contractions. He developed thrombophlebitis in his right leg during hospitalization and was subsequently anticoagulated. A slough ensued following the use of Levophed (brand of levarterenol bitartrate) in his arm and he was given penicillin, streptomycin sulfate, and Terramycin (brand of oxytetracycline). He developed signs of fluid in the right thorax and consolidation at the right lung base. Death occurred on the 36th hospital day, and was preceded by apneic episodes and disorientation.

## DISCUSSION

**D t B ke:** Was there ever any ascites or liver enlargement?

**Do t R if t i:** Apparently liver enlargement but not ascites in that his liver was palpable on admission. At least ascites was not mentioned in the report.

**D t Stru r:** The only murmur was this apical systolic murmur?

**D t R f t in:** Yes.

**D to S:** Was there any evidence of vitamin deficiency brought on by his previous alcoholism?

**D cto R if t i:** There are two things that one can mention about that. First, that the tongue, lips, and skin were described as normal.

Lt. Erwin L. Burk, MC, USN, I

Capt. George H. Rife, MC, USNR, Head Cardiology Service

Lt. L. A. Struett, J, MC, USNR, Medical Service

Lt. Robert I. Solomon, MC, USN, I

Second, according to his history he had been a chronic alcoholic but had stopped some years before his last admission here. So I think we could eliminate that.

**Doctor Cutler:** Was there any evidence of prior thrombophlebitis?

**Doctor Reifstein:** Apparently not on admission. The man had massive edema but did not have leg tenderness. It was looked for. He did have marked congestive failure, a rapid pulse, hemoptysis, spikes of fever and elevations of his pulse rate and repeatedly went into shock which occasioned the use of Levophed. I don't think there's much question but what the patient was considered to have pulmonary embolism with pulmonary infarction. One of the problems was the origin of emboli.

**Doctor Dean:** I was wondering if the thrombophlebitis resulted from the administration of Levophed?

**Doctor Reifstein:** He had a thrombophlebitis in the lower extremities before the slough appeared in the upper extremity. The Levophed was given in the upper extremity.

Well, let us try to summarize this case. There is little doubt that this man had both pulmonary and cardiac disease. Let us discuss briefly the types of pulmonary disease and cardiac disease which he might have had. Against rheumatic heart disease is the absence of history, characteristic murmurs and atrial fibrillation. In favor of the diagnosis is the patient's age but there is insufficient evidence to make this diagnosis. He had no evidence of syphilitic heart disease; there were neither murmurs nor peripheral signs to suggest aortic valvular disease. Right bundle branch block, questionable atrial enlargement (as evidenced by peaked P waves) and right ventricular hypertrophy suggest interatrial or interventricular septal defect but the history is that of sudden onset four years prior to death with repeated transient episodes of illness which is not characteristic of congenital heart disease. Beriberi heart disease is unlikely in view of the history of no recent alcoholism plus the absence of other substantiating peripheral signs. There are no clinical features to suggest myxedema. The greatly enlarged heart and episodic rather than relentless course mitigate against constrictive pericarditis (figs. 1 and 2).

Coronary heart disease remains a good possibility in a man with angina pectoris, electrocardiographic changes, progressive congestive heart failure and episodic chest pain. Our patient may have had one or more myocardial infarctions to account for his right bundle branch block and his deformed QRS complexes and again recently prior to hospital admission.

Strongly suggested by this history is pulmonary heart disease or cor pulmonale. The patient may have had an episode of pulmonary infarction with wheezing dyspnea in 1951 again nine months later.

C pt Tr y D C til MC, USN Med cal Serv  
Lt Phil p J De MC, USNR Intern



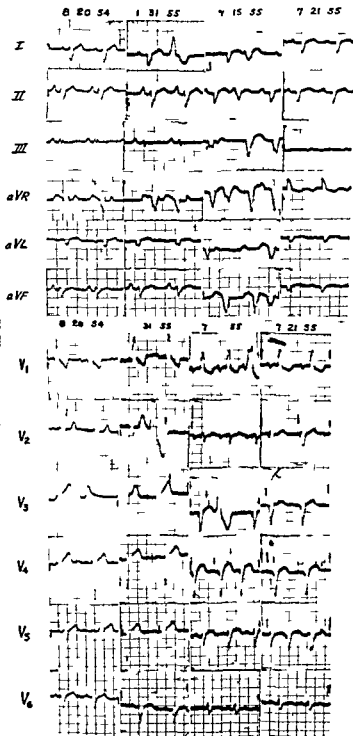


Figure 1 Electrocardiogram made on date shown, in unit divided by time of comparison.



*Figure 2 Roentgenogram on admission showing grossly enlarged heart and possible pericardial effusion.*

and then shortly before admission. Indeed, everything needed to make a diagnosis of pulmonary infarction is present—even to an x-ray shadow and the thrombophlebitis in the lower extremities. It is a clinical fact that quite often people who have antecedent heart disease may be precipitated into circulatory failure by repeated small to moderate-sized pulmonary infarctions, emboli, or thrombi; the latter perhaps arise *in situ* rather than come as emboli. Sometimes it is very difficult for the pathologist to tell whether a clot was an embolus or was formed *in situ* in pulmonary vessels. It may have occurred prior to thrombophlebitis. As many as 25 to 30 per cent of consecutive autopsies in some series have shown pulmonary infarction. This is true when full dissection of the veins of the lower extremities is carried out. Most of the textbooks warn of hip or pelvic thrombophlebitis in the presence of pulmonary infarcts. When this happens there usually is thrombophlebitis or if you wish phlebothrombosis lower down in the extremity. In fact, I think there is some evidence that some of these may actually start in the feet and work up through the calf. And that may occur before we have clinical evidence of it. Cardiac failure may be the result of obstructing sufficiently the flow of blood from the right heart so that we get right heart enlargement, edema, and also shock. The patient probably did not have any of a variety of other causes of pulmonary heart disease such as silicosis, berylliosis, asbestosis, chronic tuberculosis, or Ayerza's disease. There is a form of so-called subacute cor pulmonale occurring with carcinoma in which carcinoma of the lung

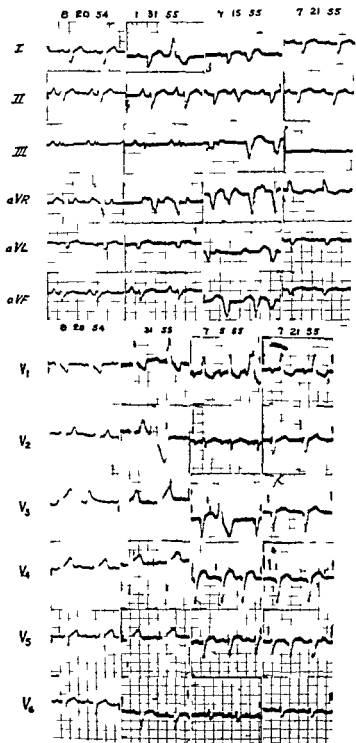


Fig 1 E1 t ardiogr m mad o d t shown, mounted by d fo compar n.



*Figure 4. Roentgenogram four weeks after admission showing the marked pulmonary congestion.*

collateral circulation through the bronchial arteries so that an infarct never forms unless the circulation is impaired as in congestive failure. I have observed clinically what proved to be pulmonary embolism in young otherwise healthy persons following fractures to long bones. This usually occurred about three weeks after the fracture often after the patient was ambulatory. The onset was sudden with severe chest pain, cough, and at times hemoptysis. Roentgenograms of the chest showed a homogeneous density usually in the lower lung field and elevation of the diaphragm. If this is not infarction, what is the pathologic condition?

**Doctor O Connell:** It is not uncommon to see in fracture cases coming to post mortem examination either directly related to their trauma or for concomitant reasons to find bone marrow emboli in the lungs. Whether or not these will be large enough to produce an infarct is the question; apparently many of them are and they can produce pulmonary infarcts in the absence of myocardial failure in spite of the dual blood supply.

**Dr. Seaton:** I've seen patients who had heart disease and sudden onset of left upper quadrant pain that was diagnosed as splenic infarct but who never came to autopsy to prove it or disprove it. I wonder if Doctor Reifenshtein would comment on that?

**Doctor Reifenshtein:** I don't know what caused the left upper quadrant pain but most of the conditions I could think of that would produce splenic infarction were not associated with the patient's condition.

either metastatic or primary may be associated with sufficient lymphatic and vascular blocking to produce a picture of death from pulmonary heart disease. I do not think that is the situation here. If this man had pulmonary emboli with pulmonary infarction as the precipitating factor for his terminal failure, we have adequate sources for such in the lower extremities and might additionally have mural thrombi in the right heart. We might also have pulmonary thrombosis, perhaps dependent on some pulmonary vascular disease, pulmonary atheromatosis or some unusual type of pulmonary vascular lesion which helped to contribute to the terminal picture. This leads us astray in the field of periarteritis nodosa. I would say that this man probably had pulmonary infarction with repeated episodes possibly due to pulmonary embolism and/or pulmonary thrombosis with enlargement of all parts of the heart, some evidence of right ventricular thickening as well as total enlargement of the heart, possibly left ventricular hypertrophy on the basis of antecedent hypertension (but which he didn't have during his last hospitalization) and coronary heart disease with possible old and recent myocardial infarction (figs 3 and 4).



Figure 3 Roentgenogram one week after admission showing bilateral pulmonary opacities on the right.

Dr. O'Connor: Would anyone else care to tender a diagnosis other than those made by Doctor Reifstein—Doctor Canada?

Dr. Canada: That pretty well covers the field. I would like to ask whether or not pulmonary infarction occurs in the absence of congestive failure? I was taught that one never sees pulmonary infarction without congestive failure. The lung has a dual blood supply. There is enough

all chambers and the hypertrophy of the right ventricle. The right ventricle averaged 0.5 cm in thickness throughout. The left ventricle averaged 1 cm in thickness. The myocardium was somewhat flabby because of the enormous dilatation but otherwise remarkably homogeneous, glistening and brownish tan. There was one small area on the posterior wall of the left ventricle that appeared slightly gray white and fibrotic but this was localized.

The liver weighed 1,800 grams and grossly was of a nutmeg type. Further gross findings included 150 ml of ascitic fluid, slight splenomegaly and dilatation and blood clots in the periprostatic venous plexus. The vessels of the calf were not examined.

Microscopic examination of the posterior left ventricle at the area of fibrosis showed the myocardial fibers separated by extensive fibrous tissue. Diffusely throughout the section the fibers were separated to a certain degree by this fibrous replacement. In addition the fibers showed numerous nuclei that are markedly enlarged and very blunted and bizarre in shape and the fibers appear hypertrophied. The right ventricle showed the same changes. The hypertrophy of the right ventricular fibers was very impressive. There wasn't quite the degree of fibrosis though it was present. Thrombosis could be demonstrated in the right auricular appendage. Figure 5 includes one of the acute

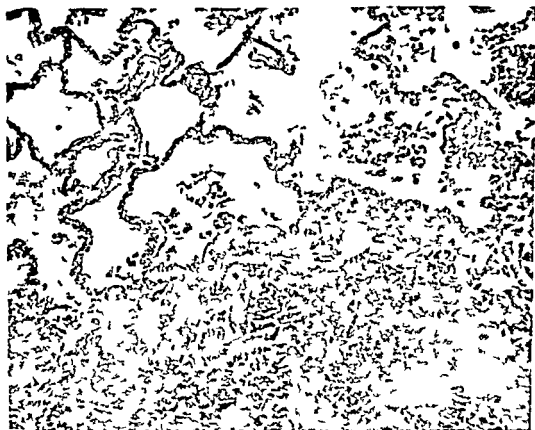


Figure 5 Photomicrograph showing sharp demarcation between an infarcted area and one of emphysema. ( $\times 100$ )

pulmonary infarcts and shows a sharp margin between the infarcted area and the more normal area. Within the more normal area an emphysematous change may be seen. Many of the interalveolar septums are blunted and gnarled and the alveolar spaces are all communicating with one another. In addition some of the vessels in this area are not infarcted. Notice the thickening of the arteriole size vessels. This thickening appears to be on greater magnification a homogeneous eosinophilic material that obliterates the media of these vessels and does not appear to be an atheromatous sort of thickening (fig 6)

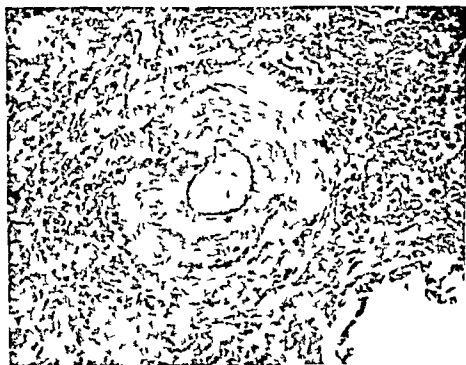


Figure 6. Photomicrograph showing marked clotted change in pulmonary artery wall ( $\times 300$ )

Figure 7 demonstrates a pulmonary arteriolar vessel occluded by a thrombus which has undergone organization and recanalization. There is fibrotic replacement of the normal pulmonary parenchyma entrapping numerous cells typical of heart failure. This represents one of the older infarcts. The fingerlike projections mentioned earlier extending into the right pleural cavity interestingly enough are small lipomata composed of mature fat with a border of condensed red and white blood cells. The liver shows a massive central necrosis of the lobules but the lobular architecture is otherwise intact. The periprostatic vein reveals early organization of an ante mortem thrombus.

In summary therefore we believe that this case represents primary pulmonary arteriosclerosis with thrombosis and infarction. The

resulting pulmonary hypertension resulted in predominantly right cardiac disease and, eventually intractable failure



Figure 7 Photomicrograph showing thrombosis of one of the pulmonary vessels with recanalization. ( $\times 450$ )

Doctor Canada What is the condition of the arteries of the rest of the body?

Doctor Johnson The systemic arteries both large and small show as I mentioned earlier in regard to the coronaries minimal atherosclerosis The kidneys were normal and the penicillar arteries of the spleen were unaffected

Doctor Canada What about the bronchial arteries? Could you identify any of the bronchial arteries?

Doctor Johnson No We've been arguing about the differentiation of bronchial arteries from pulmonary arteries for a long time but I don't think I can tell the difference

Doctor O'Connell I cannot tell either One can by dye injection methods differentiate between them grossly but not by histologic cross sections

Doctor Johnson Any other comments or questions?

Doctor O'Connell Well that's our side of the case We feel putting all the evidence together that this case meets the criteria of pulmonary arteriosclerosis There was a notable lack of associated systemic



arterial changes. The problem comes up of trying to rule out periprostatic venous thrombosis as a source of the pulmonary emboli. Many times the veins of the legs or lower extremities are the source of emboli but we feel that in this case the pathologic condition of the lung is of such a degree and extent as to have antedated any other thrombi or emboli. Terminally I think that he did have from his right heart or auricular appendage some more recent thrombi.

#### Pathologic diagnoses

- 1 Pulmonary arteriosclerosis
- 2 Pulmonary thrombosis and embolism with multiple old and recent infarcts
- 3 Cardiac dilatation and hypertrophy with myocardial failure

**D i R i f t** Usually I do not write in the report on an electrocardiogram that these findings are absolutely diagnostic of a myocardial infarction but instead say I cannot eliminate myocardial infarction or the findings are somewhat suggestive or rather suggestive or strongly suggestive of possible myocardial infarction. This probably is the result of my earlier practice in pathology. The relationship of abnormal electrocardiographic findings to pulmonary pathology is of great interest. Right bundle branch block is something rather commonly seen in right heart strain. We think of it in acute pulmonary embolism where we see transient right bundle branch block but in right heart enlargement as with for example interatrial defects, Ebstein's syndrome, pulmonary hypertension with an interventricular septal defect, patency of the ductus with an intermediate stage of reversed flow it is not at all uncommon—in fact in some of the atrial defects as high as 90 per cent of the cases may have right bundle branch block. I think the feature of greatest interest purely from an electrocardiographic standpoint is the loss of certain of the initial potentials in the precordial leads.

The occurrence of anginal distress in conditions associated with pulmonary hypertension is also of much interest and in the case we have discussed today there was no great evidence pathologically of coronary heart disease. Tinsley Harrison particularly has drawn attention to angina of this type and we have found it not at all uncommon in some of our patients with marked pulmonary hypertension.

Cases like this are most difficult to treat. When you can recognize that pulmonary infarction has occurred and do find thrombophlebitis the tendency is to consider high radical surgery. I have seen two patients in whom ligation of the inferior vena cava had been done in the hope that the change in the lung was secondary to embolism from the lower extremities. In each case the patient died. I have seen one additional case in which the patient recovered and in which I suspect that infarction was due more to embolism rather than to thrombosis.

**Doctor Norris** I'd like to say that the question of ligation of the inferior vena cava was considered on an hour-to-hour basis for quite a number of days and weeks and the last report I had was the initial autopsy report that there was extensive (pelvic vein) thrombosis. We wondered if we shouldn't have done an inferior vena cava ligation. In view of these findings, I am glad that the decision was made not to do one.

Capt Frank T Norris MC USN Assistant Chief of Medicine

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#### AMBIDEXTERITY IN SURGERY

So often practice to the surgeon consists only of learning to tie knots which the beginning surgeon assiduously practices. But how often is the practice extended to tying knots in the bottom of a container or in the corner of a deep box? Tying a knot in relatively inaccessible areas tests the real skill of knot tying. The practice should be extended to suturing and grasping small pieces of thread in improvised situations at home analogous to the so called compromised situation during surgery which after practice and with perfection would no longer be a compromised situation. The common instruments used in surgery should be handled and manipulated until their use becomes habit so that they can be properly handled and used with ease gentleness and efficiency. This can never be fully developed at the operating table without jeopardizing to some extent the patient on whom one operates.

The piano player who could use only the right or left hand well could be expected to execute only part of the interpretation of the music. The total interpretation requires the coordinated cooperation of both hands. Yet how often have we surgeons in compromised situations wished we could use our other hand to suture dissect or grasp bleeders. With practiced ambidexterity the situation would no longer be compromised.

—JOHN R DERRICK M D

from Editorial in *Journal of Medical Association of Georgia*  
pp 341-342 July 1957

# CASE REPORTS

## Xanthoma Diabeticorum

ARTHUR S LURIE *Capt*      *USAF (MC)*

**D**IABETES mellitus is a disease of protean signs symptoms and metabolic interrelationships Xanthoma diabeticorum a rare manifestation of diabetes mellitus is a result of the hyperlipemia and hypercholesteremia due to the substitution of fats for carbohydrates as the primary source of energy Occasionally a diabetic will first seek medical advice because of the eruption of the xanthoma These are elevated firm yellow papules about 1 to 3 mm in diameter which may or may not have a red halo about their base They may appear singly or in patches usually on the extensor surfaces of the extremities back of the neck shoulders upper and lower thorax and abdomen (figs 1 and 2) There is no pain associated with the eruption but there may be minimal pruritus Histologically there is fibroblastic proliferation foam cells (phagocytes with lipid droplets) and the multinucleated Touton giant cells

The disease was first described by Addison and Gull<sup>1</sup> in the year 1851 Ninety seven cases were compiled from the literature by McCavack and Shepardson in 1933 Thannhauser<sup>2</sup> and Thannhauser and Magendantz completely reviewed the subject of the lipidoses including xanthoma diabeticorum Joslin and associates mentioned the low incidence of xanthoma diabeticorum Gumpel and Lipton Margolin<sup>3</sup> and Spencer published excellent case reports

In the following case report of xanthoma diabeticorum the patient sought medical attention because of the skin eruption

### CASE REPORT

A 37 year old supply sergeant with 14½ years of military service was admitted to this hospital with suspected diabetes mellitus The patient stated that he was well until about 4½ months prior to his admission to the hospital when he had been treated with penicillin for an upper respiratory infection and sore throat Three weeks later he had recurrence and treatment at that time was with Terramycin (brand of oxytetracycline hydrochloride) because of a previous mild penicillin reaction Shortly thereafter the patient noted the onset of frequency of urination and increased thirst His appetite remained the same About

F m U S A i F    H p t a l S b l l g A i r F    B    K    D L u r i e w r t  
B to City H p t a l B    M



Figure 1 Lesions of xanthoma diabeticorum on the patient's back and neck.

three weeks prior to admission he began to note the appearance of boils on the back of his neck. One week later he noted the appearance of discrete yellow firm nodules which spread from his neck to his back, anterior part of his thorax, arms, and upper part of his abdomen. It is for this reason that the patient sought medical advice.

Past and family histories were noncontributory. There was no history of heart or kidney disease, diabetes, or tuberculosis. Systemic review was noncontributory, except for the forementioned polydipsia and polyuria.

Physical examination on admission revealed an obese white man not in acute distress. His blood pressure was 135/95 mm Hg, and his pulse rate was 80 per minute. His skin was covered with elevated papular nodules, yellow in color, firm in consistency, and located over thorax, arms, back, and thighs. The head and neck were normal. The fundi were normal, pupils round, regular, and equal, and reacted to light and accommodation. The ears, nose, and throat were normal. An upper denture was present. The chest was clear to percussion and auscultation. The heart was not enlarged, sinus rhythm was normal, P 2 equaled

## SUMMARY

The case of xanthoma diabeticorum presented is an uncommon manifestation of diabetes mellitus and is a result of the hyperlipemia and hypercholesterolemia associated with diabetes mellitus. The treatment and management is discussed.

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## THE SURGEON AND HIS HOBBIES

A good hobby an avocation that appeals to the man or woman and that gives respite and enjoyment is especially important to the surgeon with his unusual responsibilities and long hours. Avocations and hobbies are of all sorts and kinds. They vary from the sublime to the ridiculous. As long as they serve their purpose of giving congenial occupation in one's spare time it matters not what they are. Studying the theory of relativity may be at one end of the hobby spectrum collecting epitaphs from moldy tombstones at the other. A sense of humor is of tremendous advantage but a man without it can still follow a hobby but it will probably be very uninteresting to others. Of course some hobbies are far more agreeable to the family and the neighbors than others. Landscape painting stamp collecting cooking gardening and chess are less noisy than practicing on the bull fiddle or the trombone.

—ALLEN O WHIPPLE M D

in J arm l f N t l M d c l A ci t  
p 303 Sep 1957

# Acute Melioidosis

WILLIAM STEIN *Lieutenant Colonel MC USA*

NGUYEN HOAI DUC *Major MC Army of the Republic of Vietnam*

FREDERICK J LOW *Captain MSC USA*

**M**ELIOIDOSIS, a glanders like disease was first described by Whitmore and Krishnaswami<sup>1</sup> in 1912. Since then more than 300 cases have been reported in the medical literature, almost all occurring in the endemic area of the Far East.<sup>2,3</sup> Prevatt and Hunt<sup>4</sup> reviewed the literature including three cases of proved systemic melioidosis in the Western Hemisphere. Two of these were in persons who had never left the United States,<sup>2,3</sup> and the other was in a man who had been out of the country only once.<sup>4</sup> The need for recognition of this disease is increased by important military commitments in endemic areas. The case herein presented was diagnosed and followed in the military hospital of the Republic of Vietnam.

## CASE REPORT

A 40 year old Vietnamese enlisted man was admitted to this hospital 25 September 1956 complaining of abdominal pain and diarrhea. The onset of his illness was sudden with chills, fever, severe frontal and occipital headache and anorexia. Prior to his admission he had been treated for typhoid fever (the admission diagnosis) with Chloromycetin (brand of chloramphenicol).

On admission to this hospital the patient appeared acutely ill and dehydrated. His temperature was 103°F and remained elevated for five days. His pulse rate was 80 and regular and his blood pressure was 130/85 mm Hg. Examination of the chest revealed sibilant rales in both bases. The heart was not enlarged to percussion rate and rhythm were normal and there were no murmurs or palpable thrills. The spleen was enlarged but not tender. There were no palpable abdominal masses, the liver was not enlarged. The extremities were normal. Neurological examination was negative. The patient's skin was clear throughout.

Urinalyses were positive for albumin, white blood cells, 11 cells and fine and coarse granular casts. Urine cultures were negative. Blood smears were negative for parasites. Blood cultures were negative. Blood smears were negative for parasites. Blood cultures were negative. Serodiagnostic tests revealed Whitmore bacilli. Serodiagnostic tests revealed Whitmore bacilli.

negative Weil Felix and a positive titer of 1/320 for Whitmore bacilli. Sensitivity tests performed on the organisms isolated in blood culture revealed high sensitivity to combinations of Chloromycetin and tetracycline and Chloromycetin and erythromycin. Sedimentation rate by the Wintrobe method ranged from 36 to 38 mm in one hour. Blood cell counts revealed a hypochromic anemia with white blood cell counts of from 2,400 to 7,250 per  $\mu$ l and normal differential counts. Stools were negative for ova and parasites and stool cultures were negative.

Repeated roentgenograms of the chest were within normal limits. A roentgenogram of the right knee revealed extensive demineralization of the diaphysis.

Treatment with Chloromycetin was initiated on admission because typhoid fever was suspected. The patient's temperature remained elevated for five days and then decreased by lysis. Chest rales disappeared and the spleen decreased in size. Nine days after admission the patient's temperature again rose and he began complaining of severe pain in his right knee. This pain was associated with swelling and exquisite tenderness and was not relieved by salicylates. As a result of the sensitivity tests combined treatment with chloromycetin and erythromycin was instituted. Supportive treatment consisted of vitamins, blood and plasma transfusions and fluids given intravenously. This treatment was continued for four weeks with little improvement at which time cortisone was added to the therapy. Following this the patient manifested signs of mental confusion and his course was progressively downhill. He died 50 days after his admission.

**Autopsy Findings.** The liver showed areas of focal and central necrosis. The kidneys were atrophic and revealed evidence of hyalinization of the tubules, tubular necrosis and tubular nephritis. The lungs showed considerable congestion and numerous microabscesses. The spleen was enlarged as a result of congestion and there was necrosis of the malpighian bodies. The brain was not examined.

## DISCUSSION

Melioidosis, which resembles glanders in its clinical picture, is caused by a similar organism, the *Malleomyces pseudomallei*. This gram-negative bacillus, also referred to as *Pfeifferella Whitmorei*, is a small pleomorphic rod-shaped bacillus that can be isolated from skin lesions, from the blood stream and from the urine. The best method of isolating the organism is by inoculation of adult male guinea pigs intraperitoneally or by scarification of the abdominal wall with an aqueous suspension or culture of the infective material. The organism is obtained from the layers of the tunica vaginalis after 10 to 14 days. The reaction which occurs in the testis is known as the Straus reaction.

There is an acute and a chronic form of the disease. The acute or subacute septicemic form represented by our case comprises

the great majority of cases and usually terminates in the chronic form, of which only eight cases have been reported in the literature have been indigenous in the Western Hemisphere.

The acute form has a sudden onset with an incubation period varying from a few hours to three weeks. The symptoms are variable, depending on the site of localization of the infection. There may or may not be a local inflammatory reaction at the site of inoculation that is accompanied by general malaise, headache, chills, fever of an irregular type, anorexia, vomiting, diarrhea, and joint pains. Usually the local site of infection shows an early tendency to suppurate and ulcerate and as a rule the regional lymphatics and lymph nodes are involved early. From this site the infection often spreads to involve the nasal sinuses, the ears, conjunctivas and the mucous membranes of the mouth, pharynx, larynx, trachea and lungs. The septicemic form is characterized by widespread visceral involvement and prostration and death in a few days or up to three weeks is the rule. The patient usually pursues a rapid downhill course and recovery from the acute form is rare. In the chronic form the course is milder, the respiratory system is involved next in frequency to the cutaneous system and the gastrointestinal tract is rarely involved. Liver lesions have been demonstrated in 10 per cent of the cases.<sup>2, 4</sup>

The mode of transmission of the disease is not known, however, in the Far East it is believed that it is a disease of rodents and probably spread by contamination of foods with excreta of rats.

As in glanders the manifestation of the disease is varied, and the diagnosis may be difficult unless it is considered in the differential diagnosis. It is difficult to differentiate from typhoid fever, as was true in our case or from staphylococcal septicemia, erysipelas, tuberculosis, syphilis, or rheumatic fever. In the absence of skin lesions the disease may be overlooked.<sup>2, 4</sup>

There is no specific treatment for the disease. The various sulfonamides,<sup>9</sup> penicillin,<sup>10, 11</sup> streptomycin sulfate, the broad spectrum antibiotics and autogenous vaccines have been used without success. Surgical treatment with early incision, drainage of the abscesses and wide excision and cauterization of the area is the most effective method of treatment of ulcers and suspicious nodules.

#### SUMMARY

Acute melioidosis is a glanders like disease that is endemic in the Far East and may resemble typhoid fever at the onset. Transmission of the disease is probably by ingestion of food that has been contaminated by the excreta of rats. The diagnosis can be established by intraperitoneal inoculation of adult male



a cast for one month with considerable relief of the symptoms and swelling



Fig 1 (c s 1) Right gamma bow g styl d b with adjacent fl ck / calc m



Fig 2 (e 2) Th stylo d bo clearly h wn s th lateral view Th bo ot d t cily ee th a t rop st n ws.

C 4 A 37 year old woman was seen for menopausal disorders in the medical clinic at which time she mentioned that she had had pain and swelling in the right wrist on several occasions after doing heavy housework. At the time of her visit to the clinic the wrist was asymp-

tomatic. A roentgenogram (fig. 3) revealed a carpal styloid bone. No treatment was necessary.



Figure 3 (case 4) The styloid bone is shown at the base of the third metacarpal

#### DISCUSSION

One question immediately comes to mind. Is this bone a true ossicle or merely a fragment of a previously fractured styloid process? Saltzmann,<sup>1</sup> as cited by Bassoe and Bassoe,<sup>2</sup> first described the styloid bone in 1725. He considered it to be a ninth carpal bone, occurring dorsally and immediately proximal to the base of the third metacarpal. It lay between the lesser multangular and the capitate bone. He believed that it developed from an isolated ossification center in the styloid process of the third metacarpal. In the patient operated upon by Bassoe and Bassoe the bone was found to be a distinct and separate ossicle covered by cartilage on all sides save dorsally where the surface was rough for the attachment of a few fibers of the extensor carpi radialis brevis tendon. The body of the tendon passed over the styloid bone to its insertion at the base of the third metacarpal. These facts coupled with the absence of substantial trauma in the majority of cases, lead them to believe that the styloid bone is indeed a separate ossicle.

There may be several mechanisms in the production of symptoms. Zimmer<sup>3</sup> believed that a bursa develops between the tendon of the extensor carpi radialis brevis and the ossicle. It becomes inflamed either by direct trauma or repeated strain put on the tendon. Bunnell<sup>4</sup> postulated a periostitis of the bone resulting

from direct trauma. Both of these explanations seem reasonable. In the cases in which strain precipitates the symptoms, the idea of a bursa being present is most logical.

The bone may be present without causing symptoms of any kind. Pfitzner noted 16 styloid bones in 419 roentgenograms of the hand, and Bassoe and Bassoe noted 6 styloid bones in 41 roentgenograms. One of our patients (case 3) had the bone present bilaterally with symptoms in only one wrist.

The diagnosis of carpe bossu disease is made when the patient complains of pain and swelling of the dorsum of the hand coupled with the appearance of the styloid bone by roentgenogram. The lateral view with the wrist in the flexed position discloses the bone most clearly. The anteroposterior view is of little help. Occasionally small deposits of calcium may be seen in the vicinity of the styloid bone. This may represent calcific degeneration of the extensor carpi radialis brevis tendon.

Three of the four patients seen at this hospital were treated with immobilization and heat to the wrist. The symptoms subsided in two to four weeks after which there were no known exacerbations with use of the hand. The fourth patient was asymptomatic at the time of her visit and required no treatment. Bassoe and Bassoe found it necessary to remove the bone surgically in one case, the patient getting complete relief. Their other three cases were treated conservatively.

### SUMMARY

Four cases of carpe bossu disease are presented with description of anatomy and pathology of this condition. Conservative treatment produced relief of symptoms in all four cases.

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## MEDICAL OFFICER CHOSEN PRESIDENT ELECT OF AMERICAN COLLEGE OF PREVENTIVE MEDICINE

Colonel Louis C Kossuth Deputy Command Surgeon Air Defense Command has been named President Elect of the American College of Preventive Medicine at the annual college meeting in Cleveland Ohio He will assume his duties as president in November 1958



*Colonel Kossuth*

The college which accepts only United States physicians now has a membership of approximately 1 000 specialists in public health aviation and occupational medicine The college was started for the purpose of advancing education practice and research in the field of preventive medicine as well as to give aid to medical colleges in teaching preventive medicine It also supports the development of local health departments

Colonel Kossuth a native of Wheeling West Va has been on active duty since July 1941 He has served as an instructor at the Medical Officers Training School and at the Air Force

School of Applied Tactics in Florida In 1946 he was named Chief Preventive Medicine Division Headquarters U S Air Force and then in 1951 Chief of the Preventive Medicine USAF In 1954 he was appointed Head of the Department of Aviation Medicine and in 1956 was assigned Deputy Commandant of the School of Aviation Medicine his last assignment before reporting to the Air Defense Command in 1957 as Deputy Command Surgeon

Colonel Kossuth served as a United States Delegate to the First International Congress on Poliomyelitis and as a member of the U S delegation to the World Health Organization that revised the International Quarantine Regulations

## FORMER SURGEON GENERAL DIES

Rear Admiral Perceval Sherer Rossiter MC USN (Retired Inactive) died at his home in Santa Barbara Calif on 20 December 1957 He was 83 years of age



*Adm al Ro s i*

Born at Shepherdstown West Va he was graduated from the University of Maryland with a degree of Doctor of Medicine At the outbreak of the Spanish American War in 1898 he enlisted in the U S Army and after duty in Cuba served in the Philippine Islands during the insurrection returning to the United States in 1902 He was appointed Acting Surgeon in the United States Navy on 20 January 1903 and after more than 30 years of service in the ships and shore stations of the Navy was appointed Surgeon General of the Navy and Chief of the Bureau of Medicine and Surgery Navy Department on 17 May 1933 with the rank of Rear Admiral He was reappointed on 17 March 1937 and served until 1 December 1938

when he was transferred to the retired list having reached the statutory retirement age

Upon his retirement Secretary of the Navy Claude A Swanson congratulated him upon his 35 years of service in the Navy part of which were served in the highest post in the Medical Corps The letter quoted in part follows

The Department regrets your retirement from active service and takes this occasion to extend to you its heartiest congratulation and appreciation for your long and distinguished service to our Nation During the time which you have so faithfully and efficiently served you have witnessed many advancements in the morale strength and efficiency of the Navy and you have the satisfaction of knowing that you have contributed to the accomplishment of these results

Admiral Rossiter was Fellow of the American Medical Association the American College of Surgeons and the Association of Military Surgeons He was President of the Association of Military Surgeons from October 1937 to October 1938

## A MESSAGE FROM THE A M A

Fluoridation of public water supplies, free choice of physician, organization of the American Medical Association, and the Forand Bill providing hospital and surgical benefits for Social Security beneficiaries were a few of the many important subjects dealt with by the House of Delegates of the American Medical Association during its eleventh Clinical Session at Philadelphia in December 1957

Dr Cecil W. Clark, of Cameron, La., was named 1957 General Practitioner of the year after his selection by a special committee of the Board of Trustees for outstanding community service. Dr. Clark, a 33 year old country doctor who was a medical hero during Hurricane Audrey last June, was present at the meeting to receive the gold medal which goes with the annual award.

Speaking at the opening session of the House of Delegates, Dr. David B. Allman, of Atlantic City, A. M. A. President, called for "more freedom, not less, in America and in the medical profession." Dr. Allman urged the delegates to embark on local action campaigns to enlist full community support in opposition to the Forand Bill, H. R. 9467, a pending legislative proposal which, if enacted, would provide hospital and surgical benefits for persons who are receiving or are eligible for Social Security retirement and survivorship payments. The Forand Bill, he said, is "cut from the same cloth" as national compulsory health insurance and "emanates from the same minds."

The House condemned the Forand Bill as undesirable legislation and expressed satisfaction that the A. M. A. Board of Trustees appointed a special task force which is taking action to defeat the bill.

In settling the most controversial issue at the Philadelphia meeting, the House of Delegates approved a joint report of the Council on Drugs and the Council on Foods and Nutrition that endorsed the fluoridation of public water supplies as a safe and practical method of reducing the incidence of dental caries during childhood. The 27 page report on the study, which was directed by the House at the Seattle Clinical Meeting one year ago, contained these conclusions:

1. Fluoridation of public water supplies so as to provide the approximate equivalent of 1 ppm of fluorine in drinking water has been established as a method for reducing dental caries in children up to 10 years of age. In localities with warm climates or where for other reasons the ingestion of water or other sources of considerable fluorine content

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From the Council on Nutrition and Defense of the American Medical Association. This was distributed to the Department of Defense.

is high a lower concentration of fluoride is advisable. On the basis of the available evidence it appears that this method decreases the incidence of caries during childhood. The evidence from Colorado Springs indicates as well a reduction in the rate of dental caries up to at least 44 years of age.

2. No evidence has been found since the 1951 statement by the Councils to prove that continuous ingestion of water containing the equivalent of approximately 1 ppm of fluorine for long periods by large segments of the population is harmful to the general health. Mottling of the tooth enamel (dental fluorosis) associated with this level of fluoridation is minimal. The importance of this mottling is outweighed by the caries inhibiting effect of the fluoride.

3. Fluoridation of public water supplies should be regarded as a prophylactic measure for reducing tooth decay at the community level and is applicable where the water supply contains less than the equivalent of 1 ppm of fluorine.

Acting on the issue of free choice in relation to contract practice the House passed a resolution which reaffirmed approval of previous interpretations of the Principles of Medical Ethics by the Association's Judicial Council and directed that they be called to the attention of all constituent associations and component societies. One Council opinion, issued in 1927 and reaffirmed in Philadelphia, stated that the contract practice of medicine would be determined to be unethical if a reasonable degree of free choice of physician is denied those cared for in a community where other competent physicians are readily available. The resolution also cited a Council opinion, published in the 19 October 1957 issue of *The Journal of the American Medical Association* which stated that the basic ethical concepts in both the 1955 and 1957 editions of the Principles of Medical Ethics are identical in spite of changes in format and wording. This opinion added that "no opinion or report of the Council interpreting these basic principles which were in effect at the time of the revision has been rescinded by the adoption of the 1957 principles."

The 1927 Council report also pointed out that "there are many conditions under which contract practice is not only legitimate and ethical but in fact the only way in which competent medical service can be provided." Judgment of whether or not a contract is ethical, the report said, must be based on the form and terms of the contract as well as the circumstances under which it is made.

Acting on the report of the Committee to Study the Heller Report on Organization of the American Medical Association the House reached the following decisions on ten specific recommendations:

- 1 The office of Vice President will be continued as an elective office
  - 2 The offices of Secretary and Treasurer will be combined into one office to be known as Secretary Treasurer, and that officer will be selected by the Board of Trustees from one of its number
  - 3 The duties of the Secretary Treasurer will be separated from those of the Executive Vice President
  - 4 The office of General Manager will be discontinued and the new office of Executive Vice President will be established. The latter, appointed by the Board of Trustees, will be the chief staff executive of the Association
  - 5 The Council on Medical Education and Hospitals and the Council on Medical Service will continue as standing committees of the House of Delegates, but their administrative direction will be vested in the Executive Vice President
  - 6 The voting members of the Board of Trustees will be limited to eleven—the nine elected Trustees, the President, and the President Elect. The Vice-President and the Speaker and Vice Speaker of the House of Delegates will attend all Board meetings, including executive sessions, with the right of discussion but without the right to vote
  - 7 The House disapproved of the proposal to elect the Trustees from each of nine physician population regions
  - 8 The office of Assistant Secretary will be discontinued and a new office of Assistant Executive Vice-President will be established
  - 9 The Committee on Federal Medical Services will be retained as a committee of the Council on Medical Service and will not become a part of the Council on National Defense
  - 10 The Speaker of the House will appoint a Joint and continuing committee of six members, three from the Board of Trustees and three from the House, to redefine the central concept of A M A objectives and basic programs, consider the placing of greater emphasis on scientific activities, take the lead in creating more cohesion among national medical societies, and study socio-economic problems
- The accepted recommendations were referred to the Council on Constitution and Bylaws with a request to draft appropriate amendments for consideration by the House at the 1958 annual meeting in San Francisco



## COL STAPP GIVEN PUBLIC SERVICE AWARD

Colonel John P Stapp USAF (MC) recently received the Mutual of Omaha Public Service Award presented at the twenty fifth annual meet ng of the Omaha Midwest Clinical Society for his outstanding research achievements in the field of human tolerance to mechanical force and the development of protective devices and technics for with standing crash type decelerations The award consists of a plaque and an honorarium



*Shown above left to right are Dr. Joseph D. McCarthy, Colonel John P. Stapp, USAF Major V. J. Skutt and Dr. Charles F. Moon.*

The presentation of the award was made by Doctor Charles F. Moon, president of the society, in a ceremony in Omaha which included Doctor Joseph D. McCarthy, founder of the society, and Mr. V. J. Skutt, president of Mutual of Omaha. Colonel Stapp, who is chief of the Aero Medical Field Laboratory, Holloman Air Force Base, New Mexico, is the third recipient of the award. Previous winners were William Randolph Hearst, Jr. and Major Samuel Tyson, USAF.

## OFFICERS HOSTS TO MEDICAL SOCIETY



Medical officers of Fort Bragg N C and Pope Air Force Base N C were hosts recently at a dinner meeting of the Cumberland County Medical Society when Doctor Clarence E Gardner Jr (right) Professor of Surgery at Duke University was the principal speaker Also shown left to right are Colonel Paul C Sheldon USAF (MC) base surgeon Pope Air Force Base Doctor John A McKay chief neuropsychiatrist Veterans Administration hospital Fayetteville N C Doctor Richard S Kelly Jr president of the medical society and Colonel Joseph N Weaver MC USA commanding officer of the hospital at Fort Bragg The meeting was held at the Fort Bragg Officers Open Mess

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## FLYING ACCIDENTS IN THE AIR FORCE

Fourteen per cent of all the Air Force s flying accidents from 1953 1956 were listed as cause undetermined These accidents resulted in the death of 1 179 persons or 36 per cent of the total number killed during those years This thought provoking statement was made by Colonel Harry G Moseley of the U S Air Force Directorate of Flight Safety Research at a symposium on Toxic Hazards in Aviation at Air Materiel Command headquarters held 6 and 7 November 1957 at Wright Patterson Air Force Base Ohio

Those present included representatives of all the armed services the Royal Canadian Air Force and several civilian universities and industrial concerns

Most of those accidents Colonel Moseley stated "were caused by human failure The extent of toxicants is yet to be determined but they do have stature He pointed out to the 160 aero medical specialists in attendance that the pilot in his environment is subject to a great many substances that can be hostile to life These constitute some of the toxic hazards in aviation

# OFFICERS CERTIFIED BY SPECIALTY BOARDS

## Supplementary Listing

According to information from the Offices of the Surgeons General of the military medical services the following regular Medical Corps officers have been certified by the boards indicated since the listings published in previous issues of this *Journal*

### American Board of Dermatology and Syphilology

All D Smith C I USAF

J h C W l k i C pt USA

### American Board of Obstetrics and Gynecology

W l M W l k Lt C I USA

### American Board of Internal Medicine

R ym d W B l h m Lt C I USA

### American Board of Pathology

K th R D k M j USA

### American Board of Ophthalmology

L y l M Shum M j USAF

### American Board of Otolaryngology

Alb rt C D h C p USA

D l d J J ph Lt C I USA

Carl M Lin b k Lt C I USA

R b rt P Waldman C pt USAF

### American Board of Surgery

J hn A H d L C I USAF

L ur M J k Jr Lt C I USA

J hn M K y M j USA

J k B M Clur C pt USA

### American Board of Anesthesiology

R hard A R k Lt. C I USA

R h d J W d M j USAF

### American Board of Plastic Surgery

N b l M A t M j USAF

Ch l J Th Lt C I USA

### American Board of Neurological Surgery

G rd T Wan m k L C I USA

### American Board of Thoracic Surgery

(A S b d ary B d f th Am B ard f Surg ry)

W l l m H M c f J L C I USA

W l l m C Roun M j USAF

# OFFICIAL DECORATIONS

The following awards have been announced by Departments of the Army and Air Force 1 December 1957

## Legion of Merit

Phillip G Fleetwood Col USAF (MSC) James G Moore Col USAF (MC)  
Maurice J Fletcher Col MSC USA Bennie A Moress Col USAF (MC)  
James W Humphrys Jr Col USAF (MC)

## Soldiers Medal

Albina B Gdoas Capt USAFR (MC)

## Commendation Ribbon

James P Albrite Maj MC USA

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## DEATHS

DEAN Jane Sloan Captain ANC USAR of Dallas Tex stationed at Brooke Army Hospital Fort Sam Houston Tex graduated in 1939 from Baylor University School of Nursing Waco Tex commissioned a Second Lieutenant in the Army of the United States 1 January 1944 and ordered to active duty 10 January 1944 ordered to inactive duty 16 February 1946 recalled to active duty 11 December 1950 ordered to inactive duty 14 September 1953 recalled to active duty 27 March 1956 died 9 November 1957 age 44 at Dallas Tex

MARTIN Herbert Beardsley Jr Captain DC USAR of Los Angeles Calif stationed at the 665th Medical Detachment 48th Surgical Hospital Korea graduated in 1956 from the University of Southern California School of Dentistry Los Angeles Calif commissioned a First Lieutenant in the United States Army Reserve 9 June 1956 and ordered to active duty 1 July 1956 died 12 November 1957 age 29 in Korea of gunshot wounds of chest

PLATER Joseph Rue Captain DC USNR of Milwaukee Wis stationed at the Headquarters Twelfth Naval District San Francisco Calif graduated in 1928 from the School of Dentistry Marquette University Milwaukee Wis appointed Lieutenant Commander in the United States Naval Reserve 9 October 1943 ordered to active duty 1 November 1943 released to inactive duty 6 February 1946 called to active duty 15 March 1948 died 26 October 1957 age 54 at Central Emergency Hospital San Francisco Calif of coronary arteriosclerosis

RHEN Louis John Captain DC USN of Steelton Pa stationed at the U S Naval Air Station Atlantic City N J graduated in 1928 from the School of Dentistry Temple University Philadelphia Pa appointed Lieutenant in the United States Naval Reserve 23 July 1942 ordered to active duty 31 August 1942 appointed Lieutenant Commander in the United States Navy 2 April 1947 died 12 December 1957 age 51 at the U S Naval Air Station Atlantic City of myocardial infarction

## THE "ACADEMIC YEAR"

With the start of the sixth session of the Military Medicine and Allied Sciences Course at Walter Reed Army Institute of Research on 2 September 1958 10 to 15 clinicians who have completed their formal specialty training will be given the opportunity of a year of study and research in their respective fields free of the demands of the clinic or ward. The mornings in this unusual course will be devoted to round table seminars on basic scientific subjects related to medicine such as various aspects of intermediary metabolism systemic physiology host disease relationships and genetics. The afternoons will be used for study and individually selected research projects in the student's particular specialty with the help and supervision of a senior researcher in the field. Speakers at the morning sessions are to be outstanding figures in medicine from the armed services the National Institutes of Health and civilian universities and research institutions.

The small group with differing specialties the informal atmosphere and the length of the sessions (most sessions cover an entire morning) permit the discussion to develop topics completely and enable the students to become acquainted with the lecturers as well as to listen to them.

The ultimate objective is to give officers with an interest in research and teaching the additional education necessary to make them highly effective in either field or as supervisors of research or teaching activities. Auxiliary subjects such as public speaking and medical writing also are included.

The course is open to regular officers of the three services and application should be processed through channels to the appropriate Surgeon General. Brochures describing the content and scope of the course in detail are available by writing to the Assistant Commandant, Walter Reed Army Institute of Research, Washington 12, D. C.

## Reviews of Recent Books

**CURRENT SURGICAL MANAGEMENT** A Book of Alternative Viewpoints on Controversial Surgical Problems. Editors John H. Mulcolland M. D. Edna H. Ellison M. D. Stanley R. Friesen M. D. with contributions by 76 American authorities. 494 pages illustrated. W. B. Saunders Co. Philadelphia Pa. 1957. Price \$10.

The editors have condensed into one volume nearly all of the controversial surgical problems that perplex the general surgeon. It is outstanding in that each controversial point has been presented by an author who is an outstanding authority in a particular field. Each writes about his personal experience with and most present results obtained in their own practices. This volume again emphasizes the fact that a general surgeon must keep an open mind about the rationale of treatment of all diseases in which the standard method of treatment does not result in a very high percentage of cures. The only feature that is disturbing to the average general surgeon is that there are still so many diseases in which the results of surgical therapy by any of the methods presented leave a certain number of failures.

This textbook will be an excellent reference both in most small hospitals and dispensaries and should be revised at appropriate intervals to keep the surgical profession abreast of the new and changing treatment. The authors are to be congratulated in their ability to present the many facets of surgical management and to have received the co-operation of the numerous authors in this undertaking.

—S. EDE Capt. MC USN

**CLINICAL GASTROENTEROLOGY** by Eddy D. Palmer M. D. F. A. C. P. Illustrations by Phyllis Anderson. 630 pages illustrated. Paul B. Hoeber Inc. Medical Book Department of Harper & Brothers. New York N. Y. 1957. Price \$18.50.

This excellent book was originally intended for the gastroenterologist but it is the opinion of the reviewer that it would be of great value to anyone interested in diseases of the gastrointestinal tract including the internist and the general practitioner. Differential diagnosis is not covered. Eponyms are used very freely throughout the book. All parts of the gastrointestinal tract are covered thoroughly. The chapter on gastrointestinal manifestations of far removed diseases points out how diseases having no specific place in the field of the gastroenterologist may first present themselves to him.

The author stresses emotional factors in gastrointestinal disorders both primary functional disease and those diseases which carry with them an emotional aspect. In most of the sections on treatment of various diseases with emotional factors he notes that interviews with the gastroenterologist are sufficient and the aid of a psychiatrist is not necessary. In the section on ulcerative colitis where the conflicts may be deepened psychiatric aid is recommended. It is stated that

statistics on the cure of gastric carcinoma are misleading because of the failure to distinguish between the terms operability resectability palliation survival and cure The author writes It seems clear that we should give up current measures directed as cure as a bad job now without waiting for a more effective replacement A degree of emotional and physical comfort is all that can be promised the patient at the moment Perhaps the author had in mind when he recommended such a complete change of philosophy that perhaps there should be a middle of the road attitude which would be more effective from a physical standpoint

This is the most thorough book on gastroenterology that the reviewer has ever had the pleasure to read To obtain the maximum benefits from this book it is necessary that the reader have some previous knowledge of gastrointestinal diseases A bibliography appears at the end of each chapter and is very brief The illustrations and charts are excellent —EDWARD P MC LARNEY *Capt MC USN*

THE PHYSIOLOGY OF INDUCED HYPOTHERMIA Pt ed ng f Sym-  
p um 28-29 O t b 1955 d by The D of M dic l  
S N t l A d my f S N t l R a h C cl  
w th th Sp h p f The U t d St te Army N vy d Ai F r  
R b t D Drupp M D Ch m d Ed t r P bl t 451 447  
p g ll tr t d N t l A c d my f Sc ce N t n l R e h  
C un l W h gt D C 1956 P ce \$3 50

This book might be considered the primer for hypothermia the best review of available material as of 1955 The discussions after each major section make it an excellent text for teaching The review chapter for each of the five parts and the discussions serve to answer many questions raised in the individual articles and to point out deficiencies in our present knowledge A good symposium is never the result of good writing but rather intell gent editing as has been done here

The five parts follow logically one from the other Part one compares induced hypothermia with true hibernat on on a physicochemical and physiologic basis from the cellular level to that of the intact tot l organism Part two considers the effect of induced hypothermia on all the major organ systems in the body Myocardial irrit bility the major problem in the clinical application of induced hypothermia is covered in part three The clinical application of induced hypothermia in part four is the weakest point in the book It is neither a gener l summary of possible or indicated applications nor is it a series of specific applic tions but a little of each The final part covers the technics of inducing hypotherm a and problems related to each technic It includes the use of drugs as related to technics such as the lytic cocktail

The reader must remember that neither this book nor the individual articles were written as a text for do it yourself hypothermia but rather to help define the condition of the methods of and the problems of induced hypothermia And this has been very well done It is an excel lent book for all interested n th s f eld

—HENRY D GREEN *Capt MC USA*

**CLINICAL ORTHOPAEDICS** Editor in Chief *Anthony F DePalma* Number 9 The Pathologic Physiology of Metabolic bone Disorders with special section on Motorist Injuries and Motorist Safety Primary Motorist Safety Prevention of Accidents under guest editorship of *Jacob Kulowski M D* 353 pages illustrated *J B Lippincott Co Philadelphia Pa* 1957 Price \$7 50

Ninth in a series this volume presents the third and last part of a serialized symposium on Motorist Injuries and Motorist Safety "Previously volume 7 contained discussions of the Clinical Aspects" and volume 8 "Reduction of Injuries (Crash Impact Engineering)" The latest is entitled "Primary Motorist Safety Prevention of Accidents" and is of particular interest because of the direct contributions that can be made by the medical profession at large in the continuing study of predisposing factors mechanisms and preventive measures in motorist injuries

The eight papers of the first section "The Pathologic Physiology of Metabolic Bone Disorders" comprise an excellent summary of the known information of the normal physiologic mechanisms and the aberrations therefrom of the effects of hormones vitamins steroids and mineral metabolism on the skeleton Designed to present a group of unrelated papers under the heading "General Orthopaedics" the second section contains 11 papers on a variety of subjects These are not written to summarize current information on a given subject and thus provide a reference source for review but are the type of article usually appearing in medical journals One by Scaglietti and Stringa of Italy lends an international air of professional contribution which would seem worthy of encouragement for future volumes

—JOHN D BLAIR Col MC USA

**ATLAS OF EYE SURGERY** by *R Townley Paton M D F A C S Herbert M Katzin M D F A C S* and *Daisy Stilwell* Illustrator 248 pages illustrated The Blakiston Division McGraw Hill Book Co Inc New York N Y 1957 Price \$15

This book by two excellent eye surgeons and a capable medical illustrator is intended primarily as a surgical manual for residents in ophthalmology It consists mainly of drawings designed to show each operation step by step The brief text is intended only to summarize information which cannot be illustrated The visual approach is maintained on every page by 464 line drawings unmatched for accuracy and fine detail All pictures have been drawn from the surgeon's position above and behind the patient's head—the position he must take during the operation

The text is the outgrowth of the authors' long-held belief that a full set of illustrations is exceptionally helpful in teaching the fine details of surgical procedures The excellent detailed presentation of the subject of corneal transplantation in this manual reflects the interest of the authors rather than the frequency of the operation An interesting and helpful feature is an Index of Instruments and Notes on Instruments



A typographical error was noted under figure 438 dealing with controlled tenotomy of the superior oblique muscle. The legend states that the sheath of the superior rectus muscle is longitudinally incised where as this should have been superior oblique. It is the feeling of this reviewer that the technic of tucking the tendon of the superior oblique medially to the superior rectus muscle might result in the tuck being too close to the pulley of the superior oblique thus limiting the gaze of the eye downward and inward. By tucking the tendon temporarily to the superior rectus muscle this complication cannot occur. In the discussion of the technic of evisceration the size of the implant was not mentioned. It seems important to the reviewer that the implant be smaller than that used in enucleation so that the eviscerated eyeball will not be too large for a prosthesis.

The authors are to be congratulated for presenting a remarkable new book illustrating the technic of eye surgery. The visual approach is a new and most effective means of teaching the subject of eye surgery. It is recommended for every resident in ophthalmology and it will be helpful to the experienced ophthalmic surgeon especially to those who teach surgery.—KARL J. PALMBERG *Capt MC USA*

HUMAN BLOOD COAGULATION. Edited by R. M. Bagg. B. S. (London) Ph.D. (Toronto) M.D. (London). Ed. R. G. MacFarlane. M.A. (Oxford) M.D. (London). F.R.S. 2d edit. 476 pages. Illustrated. Churchill Livingstone. Philadelphia. 1957. Price \$8.50.

There has been great progress in research on blood coagulation in recent years and the topic is well covered and correlated in this volume on blood coagulation. In this field knowledge and theories are constantly changing making it difficult to write a coherent and interesting text. However the authors have achieved a valuable and readable account of the subject. The volume covers in an extensive manner all phases of blood coagulation. It is highly recommended to all who are interested in blood coagulation either as a reference or as a laboratory manual.—V. E. MARTENS *Capt MC USA*

MEDICAL NURSING. by Amy F. Brown. R.N. B. Ed. M.S. Ph.D. 3d edit. 947 pages. 447 illustrations. 42 color plates. 32 figures. W. B. Saunders. Philadelphia. 1957.

The author has written a compendium of medical illnesses and the nursing care involved in the care of medical patients. Much research and organization have gone into the preparation of this text. Its presentation is simple, direct, factual and richly illustrated. There are liberal quotations from and references to medical text, medical and nursing journals and periodicals of allied fields.

Students accustomed to educational methods involving library research, creative thinking and the application of scientific principles and problem solving may find this textbook too didactic and factual even though directed to them. The older graduate nurse might find this book of interest and value as a general review text in medical nursing.

As a medical nursing text its value would be enhanced if there were more emphasis on the nursing arts involved in meeting the problems encountered in the home as well as the hospital in the neonatal diseases and the diseases of maturity and old age. Miss Brown has thoroughly covered the medical and nursing aspects of diseases of the nervous and locomotor systems and communicable diseases of bacterial and nonbacterial in origin. There are individual chapters devoted to poliomyelitis and pulmonary tuberculosis.

By way of introduction to each chapter worthwhile problems for the student to consider are presented. The bibliography and references are current and the appendix includes an excellent listing of agencies and their locations specifically related to rehabilitation, home care programs in long-term illness, the aged, cancer, diabetes, and diseases of the nervous system. Students and instructors would find this a complete and ready medical reference.—EVELYN M. BEDARD Maj USAF (MC)

**HUMAN BLOOD GROUPS AND INHERITANCE** by Sylvia D. Lawler M.D. and L. J. Lawler B.Sc. with a foreword by R. R. Race Ph.D. M.D. C.S. (England) F.R.S. 103 pages illustrated Harvard University Press Cambridge Mass. 1957 Price \$1.50

Here is a clear, compact, and sound discussion of the human blood groups and their hereditary bases. The rich background of the authors, who are British researchers of international repute, is demonstrated in stimulating fashion. Following a historical survey, a lucid description is given of red cell antigen and antibody behavior upon which blood grouping techniques are based, and suggestions are included for organization and methods in the laboratory. The chapters on the heredity of blood groups resolve many questions on the exact manner of inheritance of normal human characteristics. The material on genetics is readily understandable even to a reader with little or no background in this field. The ways in which isoimmunization to the Rh factor occurs, the role of sensitization in hemolytic transfusion reactions, and in the causation of hemolytic disease of the newborn are very well covered. Although a bibliography has not been included, the indexing and the glossary are more than adequate. This manual should be exceptionally useful, particularly in the training of new personnel in the organization of a blood grouping laboratory.

—JOSEPH V. MICHALSKI Maj USAF (MSC)

**FLUID AND ELECTROLYTES IN PRACTICE** by Harry Statland M.D. 2d edition 229 pages illustrated J. B. Lippincott Co. Philadelphia Pa. 1957 Price \$6

The second edition of this volume has been designed as a teaching primer, not as a source book. This purpose has been accomplished at the risk of oversimplification and avoidance of controversial matters. An example of the latter is a concise description of the author's procedure for intestinal lavage as an adjunct in the management of renal shutdown, without reference to continuous gastric suction preferred by

certain other authorities in this field. Similarly no mention is made to Scribner's recently published concept (1956) of the relationship between changes in total body potassium and changes in the capacity for storage of potassium and the more critical interpretation of the serum potassium related thereto. Even though revision of the section on metabolism and renal excretion of potassium constitutes a major change in this second edition the author does not clearly state that acidosis increases and alkalosis decreases the serum potassium level independently of changes in the potassium content or capacity. Notwithstanding the foregoing as a practical guide this small volume continues to meet the widespread demand for a succinct account of the physiology and pathology of the body fluids.

—H LEONARD JONES J Capt MC USN

KAPOSI'S SARCOMA M It pl Id p th H m t h g c Sar om by S m l  
 4 Bl Jarb B S M D F A C P Am a L ture Se  
 Publ: t on N 308 A M g ph Th B a t t e D v f  
 Am t can L ctur D m t l g y d t d by A th C C rt M D  
 171 p g Ilu t d Charl s C Thom P bl h Sp gf Id  
 Ill 1957 P \$5 50

This monograph is the initial volume of a series of studies on the cutaneous manifestations of the diseases of the reticuloendothelial system. The pages of this small well printed and diffusely illustrated volume contain a concentration of knowledge concerning Kaposi's sarcoma (multiple idiopathic hemorrhagic sarcoma) not to be found in any other work. From the historical aspects through the etiology pathology symptoms diagnosis and differential diagnosis prognosis and treatment one is impressed by the amount of work represented. The publications on this subject have been covered comprehensively (291 references) and condensed into an easily read work that contains the present knowledge of the subject in a readily available form. The chapters on diagnosis and differential diagnosis prognosis and treatment alone are worth the price of the book to any who are dealing with this rare and somewhat controversial disease. Most dermatologists will want to add this work to their libraries and it should certainly be available on the shelves of all reference libraries.

—JOHN D WALTERS Capt MC USN

THE PHYSIOLOGY AND BIOCHEMISTRY OF LACTATION by S J F Il y  
 D Sc Ph D F R S 153 pag Il t t d Ch l s C Th m  
 P bl h t Sp gf Id Ill 1956 P \$3 75

This is a series of lectures given by the author in 1953 dealing with the physiology and biochemistry of lactation. The majority of the subject matter pertains to advances in the dairying industry. There is a wealth of information on the application of fundamental knowledge of hormonal control of the mammary gland to artificial stimulation of udder growth and lactation in cattle. Inasmuch as the dairy industry provided the main stimulus for the author's investigations it is not surprising that a significant portion of the volume is concerned with

factors that will increase the quality and quantity of milk. Of clinical application are the sections dealing with the development of milk secretion (lactogenesis) and maintenance of milk secretion (galactopoiesis). The pertinent literature dealing with the effects of adrenal, thyroid and pituitary function on these processes is thoroughly reviewed. The important role of growth hormone in galactopoiesis is covered in detail, most of the work in this area having emanated from the author's own laboratory. The discussion in these areas is authoritative and comprehensive and based on extensive personal experience as well as thorough familiarity with the literature. The two final chapters are devoted to the biochemistry of milk fats and protein and the origin of lactose. This volume will undoubtedly remain for many years as the definitive text on this subject. While its appeal is not primarily to the practicing physician, those concerned with gynecologic endocrinology will find it a valuable addition to their libraries.

—PAUL J. ROSCH *Capt MC USA*

**DEGENERATIVE CHANGES IN THE STERNOCLAVICULAR AND ACROMIOCLAVICULAR JOINTS IN VARIOUS DECADES** by *Anthony P. DePalma*, M.D. American Lecture Series Publication No. 309. A Monograph in The Bannerstone Division of American Lectures in Orthopaedic Surgery, edited by *Charles Weer Goff*, M.D. 178 pages, illustrated. Charles C. Thomas, Publisher, Springfield, Ill. 1957. Price \$5.50.

This unique and scholarly monograph is an important contribution to medical literature. The author has described pathologic and normal anatomy of the acromioclavicular and sternoclavicular joints in great detail in the various decades of life. The book has many fine photographic reproductions of dissected specimens and of microscopic appearances of specimens of various ages. The functions of these joints are described to give a better understanding of clinical abnormalities.

This work will be of assistance to clinicians who treat disorders of these areas. In the past these joints have not been well understood but with this excellent presentation orthopedic surgeons will have better understanding of the pathology of these areas. The bibliography is complete. The book is highly recommended to those in the field of orthopedic surgery and would be a valuable addition to a library of anyone interested in this subject.

—ALFRED O. HILDOBLER *Lt Col MC USA*

**THE YEAR BOOK OF ENDOCRINOLOGY (1956-1957 Year Book Series)** edited by *Gilbert S. Gordan*, M.D., Ph.D., F.A.C.P. 377 pages, illustrated. The Year Book Publishers, Inc., Chicago, Ill. 1957. Price \$6.75.

Today's well rounded endocrinologist must be a clinician first but must also be well versed in pharmacology, protein and steroid chemistry, intermediate carbohydrate, protein and fat metabolism as well as radioisotope and laboratory techniques. Fortunately Dr. Gilbert Gordan possesses all these capabilities and the best evidence is this ar-

book which like its predecessors continues to be one of the most valuable reference guides to current endocrine thought. The present volume abstracts about 400 articles dealing with a variety of endocrine subjects that appeared during the calendar year 1956. While the majority of articles come from American and British journals, a number are gleaned from specialty journals not usually read by the endocrinologist or internist, and others are obtained from foreign publications. The abstracts are objective, concise, and accompanied by the original illustrative material when indicated. Valuable critical editorial comments occur after selected articles which often help to explain the significance of the results, or to place the findings in proper perspective in view of prior or subsequent studies.

The book is divided into chapters dealing with specific endocrine glands, and each chapter begins with a preface surveying recent developments in that particular field. There also are two special articles.

Thyroid Hormone Transport by Albright and Larson and Glucagon Recent Developments by Elrick, which further explain new trends in these areas, and are in keeping with the high caliber of the volume in general. There are certain articles which might have been excluded, and others which might have been included, but this is a personal matter, and Dr. Gordan's judgment results in a very fair cross section of the important material. This volume is the best answer to the problem of maintaining contact with an ever increasing literature. It may be that future years will see separate Yearbooks of Clinical Endocrinology and Endocrine Research, just as the Endocrine Society has found it necessary to publish two separate journals. Till then, the present volume serves both functions admirably, and remains indispensable to the endocrinologist or internist with interest in metabolic disorders, as well as a tribute to the unique talents of its extraordinarily capable editor. —PAUL J. ROSCH, Capt., MC USA

THE DIAGNOSIS AND TREATMENT OF PULMONARY TUBERCULOSIS by  
 Paul D. / It M D with h pt on P th l gy by A Rey l d C  
 M D d P lmonary Fun t by O c F l M D 2d ed t  
 426 p g 162 ill t t d l pl te i c lor L & F b g Ph l  
 d lphi P 1957 P c \$9

This book covers the problem of tuberculosis in a concise, accurate, and practical manner. As a second edition, it provides an up-to-date reference on current treatment and diagnosis. No attempt is made to provide a solution to the many controversial concepts in drug therapy. In regard to this, the author states: "These problems are under study, and solutions are being worked out. In the meantime, it is well to be aware that chemotherapy for tuberculosis is constantly changing and progressing."

Despite the fact that the popular attitude towards tuberculosis may be limited to a concern of current chemotherapeutic and surgical means, the authors present a scientific document on all aspects of pulmonary tuberculosis. They have assembled under one cover 1,600

tory methods in diagnosis physiologic tests and radiologic patterns of disease tissue pathology and tests of organism susceptibility and resistance. In this material many fine illustrations have been used illustrating the segmental anatomy of the lungs. The chapter on allergy and immunity is well presented. Concepts are made meaningful by concise writing. The book is written with mental and emotional aspects of patient management in mind. It is brief but intensely practical and offers techniques of management directly related to the reality of the doctor's day.

—JAMES C. SYLVESTER, M.D.

**SURGEONS ALL** by Harvey Graham, M.D. Foreword by Oliver W. Fisher, M.D.  
459 pages illustrated Philosophical Library, New York  
Price \$10

This volume presents a kaleidoscopic picture of the surgeons through the world's known history. In capsular form it presents the contributions of the ages to the surgical art with an able emphasis on our English, Scottish, and French medical and surgical forebears.

The reader is duly impressed with the considerable experience of the earlier surgeons obtained on the field of battle and the obstacles which confronted them. The difficulties in the treatment of fractures, wounds, and burns are interestingly woven into the history of the art of surgery. Some of the clandestine activities of the executioners are presented in a witty fashion. This colorful picture of the present in England for 300 years became defunct with the passage of the Anatomy Act of 1832.

The reader is held in awe on the professional and extracurricular activities of such men as William Harvey and John Hunter and their tremendous capacity for work almost unheard of in this age. They dissected many hundreds of different species of vertebrates in order to learn anatomy and physiology. One is forced to reflect and compare these activities with our contemporary courses in comparative anatomy.

Today in aviation medicine we ponder the problems of the high altitude and thermal barriers while prior to 1840 surgeons both in America and Europe were trying desperately to pierce the twin barriers of hemorrhage and sepsis which practically limited them to amputations and ligatures. The author with justification dwells considerably upon Lister and his contemporaries and impresses the reader of the new vistas in surgery which were opened by his antiseptic techniques and Crawford Long's discovery of ether. American readers perhaps would have liked to see more written on the contributions of such pioneers as Hal Kelley, Cushing, and Graham.

There is an outstanding bibliography which can be readily used for a more precise study of a given individual or era. **Surgeons All** is well recommended for leisure reading. —PAUL V. DAVIS, Col. USAF (M)

DENTAL CLINICS OF NORTH AMERICA Symposium on Emergencies  
 Dental Practice July 1957 617 pages Illustrated by B. Sunders Co. Philadelphia  
 Price \$14.00 per copy (only a very few of  
 3 numbers—March, July, and November)

This is a compilation of 22 articles submitted by different authors specifically for this publication devoted to the management and prevention of emergencies in the practice of general dentistry and oral surgery. All of the contributors are sufficiently well known to lend scientific merit to the volume and each article is concise so that reading is easy.

If only one outstanding point were to be retained from this reading it would concern the priority given to oxygen therapy in the management of untoward reactions in the dental office to drugs, anesthetics, and syncope. There appears to be general agreement that every dental operating room should have ready access to oxygen apparatus and therapy.

The general theme of the text is worthily repeated by several of the contributors: the best way to treat emergencies is to prevent them. Hemorrhagic problems are adequately surveyed from the standpoint of prevention and treatment. Some of the complications presented by systemically ill patients to dental treatment are analyzed with the thought of prevention but emergency treatment procedures are given. Various accidents related to dental operative procedures are viewed through the eyes of those experts required to provide corrective measures.

The management of problems in oral trauma are well presented. Seldin's article on the Management of Pregnant Patients in Dental Practice is authoritative, current, and particularly well done. The articles on the medico-legal aspects of dentistry and the role of the dentist in treating mass casualties also require particular commendation.—THEODORE A. LESNEY, Captain, DC, USN

PLASTIC ARTERIAL GRAFTS by W. Sterling Edwards, M.D. 126 pages  
 Illustrated by C. Th. M. P. Bl. h. Sp. ingf. Id. Ill. 1957  
 Price \$4.50

This 102 page monograph on plastic arterial grafts is a review of the history, development, technique and problems of artery blood vessel replacement by various methods. Brief reference is made to the diagnosis and treatment of acute arterial injury, the management of aneurysms, segmental obstructive arteriosclerosis, and the surgery of the thoracic aorta.

The monograph is well written and well illustrated. Numerous references are made to the writings of other investigators so that a very thorough bibliography may be found.

In essence, however, the principal theme of this monograph is the crimped nylon tube. This is understandable since the author has played an important part in the development and in the clinical application of this prosthesis. The biggest objection by other investigators to the use

of nylon as a material for an arterial graft is the loss of tensile strength and deterioration of nylon after implantation Dr Edwards admits his own confirmation of these findings but with what he considers to be important modifications He reports one experiment where the nylon tape used to tie the graft in place shredded like wet tissue paper yet the tensile strength tests of the graft itself showed no loss in tensile strength He offers no explanation for this discrepancy in nylon degeneration but considers several variables dealing mainly with the size of the filaments in the material used the chemical modification by formic acid and also the use of silicone solution in treating the nylon tubes At any rate further investigation is needed before any definite conclusions can be arrived at

*Great strides have been made in the past five years in blood vessel replacement by homografts and synthetic materials thanks to the efforts of such investigators as Dr Edwards The ultimate solution will surely be found but this will take time*

The author's closing statement honestly summarizes the development of the crimped nylon tube as "only a step in the direction toward a final and ultimately ideal arterial graft" The statement only emphasizes further the feeling of the reviewer that the book has been prematurely published This is unfortunate since a potential value has been lost because of the lack of proof that only time can give

—FERDINAND V BERLEY Capt MC USN

PROGRESS IN NEUROBIOLOGY II Ultrastructure and Cellular Chemistry of Neural Tissue edited by Heinrich Waelsch M D with 37 participants Series Editors Saul R Korey M D and John I Nurnberger M D 249 pages illustrated Paul B Hoeber Inc Medical Book Dept of Harper & Bros New York N Y 1957 Price \$7.50

This publication reports a symposium sponsored by the American Neurological Society and the Western Reserve University School of Medicine Major emphasis is on chemical constituents of neural tissue in terms of their intimate cellular distribution as well as changes observed under physiologic and pathologic conditions There is a discussion of ultrastructure as observed in the electron microscope and to impulse events related to synaptic activity and active secretory functions The subject material is presented in lecture form followed by a list of essential current references and by a discussion of panel members Each subject is covered by direct contributions from research investigators in the field Methods of other investigations are revealed in the various discussions and tables extending investigative data are inserted in various areas throughout the text There are 12 chapters in this volume covering the cellular chemical aspects of neural tissue This publication would be of particular interest to biochemists and physiologists who are concerned with laboratory investigations involving neural tissue but is of less value than the original published reports —WILLIAM H LEE Lt Col USAF (MSC)



HISTOLOGY by *Arthur Wothelm M B F R S C 3d dit* 895 p g s  
 582 figures number included 8 plates 1 large 1 small J B L pp cott  
 Co Phil d lph P 1957 Pr c \$11

This standard textbook histology is written by a noted educator primarily for the use of students. The popularity of the book is well attested to by the need of a third edition within five years of its first publication. The latest edition differs from the second edition of 1953 by some augmentation and deletions in the text in order to incorporate results of recent research by the inclusion of a number of beautiful and instructive electron micrographs and by having an up to date bibliography appended to each chapter. The value of the book for a medical officer rests on the comprehensive treatment of the subject matter and the excellent bibliography —*HELMUTH SPRINZ Lt Col MC USA*

OCCIPITOPOSTERIOR POSITIONS by *Edward L K g A B M D F A*  
*C S F A C O G Am r L ture S P bl cati N 310*  
*A M graph Am r c L tur Gy l gy d Ob t t dit d*  
 by *E C Hamble B S M D F A C S 106 p g 11 trat d*  
 Ch l C Th m P bl h Sp gfi ld Ill 1957 P \$3 75

This readable well illustrated small volume brings together practically all of the methods of handling occipitoposterior positions as well as discussions of etiologic factors involved differences in labors with these positions and the results of treatment. The methods of management both operative and nonoperative are presented and illustrated in detail. The nonoperative methods described include positioning on the side to which the occiput points use of the knee chest position and manual rotation as described by Danforth Pomeroy's and Melhodo's methods using manual rotation and forceps also are presented using the original illustrations.

The operative methods of Smellie discovered in his use of the forceps is quoted verbatim as are Scanzoni's and Kielland's original descriptions of their operations. Seides two forceps maneuver and Bill's modification of the Scanzoni procedure are included as well as the authors methods and opinions. The use of Barton forceps as described by Barton Caldwell and Studdiford is summarized and is illustrated by some very nice redrawings from their original article. Other operations described by DeLee and Greenhill Merchan of Colombia and Maughan are presented in sufficient detail for clarity. The forceps of Mann and of Jacobs and their use are included for those interested.

The author's attention given to (1) correct diagnosis (2) proper evaluation of the pelvis (3) consideration of cephalopelvic disproportion (4) insistence on spontaneous labor with careful observation (5) allowance of adequate time for spontaneous anterior rotation (6) adequate maternal support (7) conservatism with stimulation (8) appropriately selected operative intervention and (9) thorough knowledge of operative technic made this a welcome addition to the obstetric literature —*DWIGHT A CALLAGAN Capt. MC USN*

**HORMONAL REGULATION OF ENERGY METABOLISM** compiled and edited by *Laurance W Kinsell* M D 242 pages Charles C Thomas Publisher Springfield Ill 1957 Price \$5 25

This book contains the proceedings of the 1956 Metabolic Conference and includes reports on carbohydrate metabolism enzymatic control pituitary hormones the thyroid insulin and the adrenal cortex. It is of interest to read the expression of the foremost authorities in the field of metabolic research and to sense the challenge of problems to be resolved. The book is advertised to be of interest to "clinicians clinical investigators and fundamental scientists" but for the practicing clinician it may seem far afield from matters of practical value. There is little information which will aid in patient management but physicians interested in the fields of metabolism and endocrinology may be challenged by some facet of research.

—FRANCIS G SOULE Jr Capt MC USN

**THE YEAR BOOK OF DERMATOLOGY AND SYPHILOLOGY** (1956 1957 Year Book Series) edited by *Rudolph L Baer* M D and *Victor H Witten* M D 464 pages illustrated The Year Book Publishers Inc Chicago Ill 1957 Price \$7

This book an annual publication is a good review of the current dermatologic literature. It is a valuable source of information to keep one abreast of the times and should be well accepted by the profession. The entire field of dermatology and syphilology is well covered. It is noted that syphilis is still with us and a review of the advances made in this disease is very timely especially when some people are likely to sit back and relax when an almost sure cure for a disease is discovered.

The first 107 pages are given over to a very prevalent condition allergic eczematous contact dermatitis and this subject is especially well treated especially the therapy of this type of dermatosis. The chapter on drug eruptions is timely and it is noted that some of the newer drugs are still not "wonder drugs" and that some of them might be more common sensitizers than we realize at present. The chapter on "Cancers precanceroses Other Tumors" serves as a reminder that one should be concerned with the layers of the skin as well as its outer surface. Another on fungus diseases is short but gives the pertinent facts of diagnosis and treatment of this prevalent dermatosis. More than 100 pages are devoted to investigative studies. In this portion of the book the various "subfields" of dermatology receive their just recognition. This section might well occupy a separate book.

The scientific merit of this publication can not be questioned. The authors have achieved their aims. The major shortcomings lie in the inclusion of too many individual case reports and too many descriptive terms in an already confused nomenclature. The book is not recommended for anyone who has not had at least some formal training in the field.

—JOHN H COX Capt MC USN

tis but none have been as complete and thorough as this one. A number of these patients have been under careful study for over twenty years.

It has indeed been a monumental task and the authors are to be complimented for the painstaking and accurate reporting of this crippling and disabling disease. There are many outstanding chapters in the book two stand out in particular the one on Diagnostic Criteria and the one on Subsequent Courses of the Disease. Each chapter is annotated with an excellent summary giving in clear and concise language the high points contained therein with a closing paragraph indicating objectives for further study. The general practitioner may not consider this book to be of great value because of the absence of a section on therapy however I am certain he will find the book interesting and rewarding. To the internist interested in rheumatology and to the rheumatologist this book will be a valuable adjunct to his office library as it is a veritable treasure house of information about the less well defined and controversial points pertinent to rheumatoid arthritis. —LEON J. NUMAINVILLE, C. I. MC USA

PEDIATRIC CLINICS OF NORTH AMERICA August 1957 Symposium  
 Handicapped Children: The Problem of the Child with Mental Defects  
 Edited by 799 pages Illustrated with 100 Photographs  
 Price 1957 Price \$15 per copy of the book and quarterly Serials  
 Published by Yearly Publications Company

This is primarily a symposium on handicaps and their prevention in children. There is a statement on the responsibilities of the medical profession in the use of x-rays and other ionizing radiation and an article on the surgical management of total bile duct atresia based on a case surviving four years. The symposium on handicaps and their prevention was thoughtfully organized but of necessity each individual section was limited. The section on perinatal factors is timely and another on immunization procedures is a concise review of present practices richly documented.

The chapters on visual hearing and dental defects are well presented short reviews reminding practitioners of the problems in their respective fields and with an appeal for early referral to the appropriate specialists. The discussion on social and emotional handicaps is a pleasant readable summary of the psychologic problems of the growing child and an appeal to the medical educators to improve the physicians training in this area is appropriate. The section on education and training of children with handicaps emphasizes our present all out trend to train every child to a median. The editor's summation of the community's responsibility to the handicapped child re-emphasizes the purpose of this clinic i.e. to stimulate greater interest in the problems of the handicapped among those physicians caring for children and to re-emphasize the necessity of the team approach to the total care of the child. —JOHN P. FAIRCHILD, C. I. MC USA

TEN MILLION AND ONE Neurological Disability as a National Problem, Arden House Conference Sponsored by *The National Health Council* 102 pages Paul B Hoeber Inc Medical Book Dept of Harper & Bros New York N Y 1957 Price \$3.50

This book is a conference report which originated from a meeting of experts in the field of neurologic disease and rehabilitation at Arden House in Harriman New York during December 1955. The symposium was sponsored by the National Health Council. The chapters contain the conclusions and recommendations obtained from group discussions of the various major sections of the problem. The volume will be of little interest to military medical officers not concerned with neurologic diseases. However for specialists in the field including physicians physiotherapists occupational therapists and social workers the material presented will give a clearer idea of the magnitude of the neurologic disability program and what experts believe may be done to make management study and treatment in this field more effective and complete. —ARTHUR L. SCHULTZ Capt MC USN

ANNALS OF THE NEW YORK ACADEMY OF SCIENCES Volume 71 Art 1 Pages 1-292 July 10 1957 editor-in-chief Otto V St Whitelock. The Effects of the Sulfonyleureas and Related Compounds in Experimental and Clinical Diabetes Conference Chairman and Consulting Editor, Rachmiel Levine 292 pages illustrated The New York Academy of Sciences New York N Y 1957 Price \$4

This is a collection of papers by eminent workers presented at a conference on the hypoglycemic sulfonylureas held by the New York Academy of Sciences in February 1957. There is an introduction to the volume and concluding remarks by Rachmiel Levine the conference chairman and consulting editor of the monograph.

These papers begin with a history of the discovery and development of the hypoglycemic sulfonamides beginning in 1942. Detailed and ingenious experiments follow in papers exploring and discussing the possible mode of action of carbutamide and tolbutamide. The discussions usually are models of logical thinking and deduction. They provide the reader with information about the effects of the compounds on insulin  $\text{P}^{131}$  degradation *i.e.* on insulinase peripheral glucose utilization on the two intermediates of glucose metabolism pyruvate and lactate the hepatic glucose output on the beta cells and other metabolic processes. Several authors discuss the effect on pancreatic morphology. There are toxicological studies and a number of papers on the clinical experience with these agents.

The volume is most informative and interesting even though it requires more than an average amount of concentration and time. It is excellent reading for the research worker and exciting for the clinician specializing in metabolic disorders. An extensive bibliography following each paper will enable the investigator to acquire even more detailed knowledge about the problem. This is also an up to date authoritative and compact source of reference.

—M. M. DRISKELL, Capt MC

An In t r d c t n to BLOOD GROUP SEROLOGY Th o y T h n q P r c  
t c l Appl t App t by K t h l E B r m d B b  
E D d d M S (L d ) P b D (L d ) 317 p g 30 Il t r a t o s  
L t t l B w & C B t M 1957 P i e \$7 50

During the past year a number of books have appeared dealing with various aspects of the rapidly growing and fascinating field of immunohematology. One text concerns itself with the blood groups and their inheritance, another with racial distribution, another with technical methods, another with blood group substances, and another with clinical implications. The authors of this volume set as their objective the task of compiling a textbook that would deal with all aspects of immunohematology in order to give a general picture with detailed operation of an immunohematologic laboratory. To accomplish this a threefold approach was used: theory, technic, and laboratory and bench organization. The authors are quite capable of accomplishing such a work. Both are well grounded in the skills of blood group serology and have actively participated in the investigation of many practical and theoretical problems that have developed as the science has progressed. The book is divided into six sections and three appendices. Generally it is designed as a reference book for those engaged in routine and special blood group serology. As a guide for those who do not specialize in this type of work, a special table of contents is included recommending certain specific portions of the book that will be useful. The authors have accomplished their task of presenting the plans of the safe and competent handling of a large volume of work. For this reason alone it is highly recommended.

—JOSEPH H AKEROYD Lt Col MSC USA

PNEUMOENCEPHALOGRAPHY by E G m R b t M D (M l b ) F R  
C P F R A C P 482 p g Il t t d Ch l C Th m P b  
I h Sp g f eld Ill 1957 P r c \$14 50

This work presents a well rounded prospectus of pneumoencephalography. The first section is devoted to the physics or mechanics and this is followed by an informative section on the technical aspects with attendant difficulties and rectifications. The next sections deal with respective regions such as posterior fossa, cerebral aqueduct, third ventricle, suprasellar area, and lateral ventricles, followed by a chapter on deformities of the lateral ventricles as the result of expanding lesions, and in turn is succeeded by a short chapter that treats of neoplasm investigation in the cerebral hemispheres. Other illuminating chapters include head injuries, infections, atrophic lesions, vascular diseases, hydrocephalus, and developmental anomalies.

There is considerable sagacity in this book, probably the result of the author's extensive neurologic background. It is best reflected in those parts devoted to diagnostic difficulties, studies in children, or the value of pneumoencephalography. The book is a considered basic requirement for those in radiology, neurology, or neurosurgery. The bibliography is excellent as well as the diagrams and the other illustrations. —RICHARD R CAMERON Col MC USA

## New Books Received

Books received by the *U S Armed Forces Medical Journal* are acknowledged in this department. Those of greatest interest will be reviewed in a later issue.

- MEDICAL DEPARTMENT** United States Army, Surgery in World War II Ophthalmology and Otolaryngology Editor-in-Chief, Colonel John H. Coates Jr MC USA Editor for Ophthalmology M. Elliott Rand Lt M D Editor for Otolaryngology, Norton Canfield M D Associate Editor Elizabeth M. McPetridge M A 605 pages illustrated Historical Unit Army Medical Service, Office of the Surgeon General, Department of the Army Washington 25 D C 1957 For sale by the Superintendent of Documents, U S Government Printing Office Washington 25, D C Price \$4
- CARDIOVASCULAR REHABILITATION** edited by Paul Dudley White M D, Howard A Rusk M D, Bryan Williams M D and Phillip R. Lee M D 155 pages The Blakiston Division McGraw Hill Book Co Inc, New York N Y 1957 Price \$6.50
- The Physiologic Basis of GASTROINTESTINAL THERAPY** Selected Topics by Heinrich Necheles M D Ph D F A C P and Martin M. Friesen M D F A C P 330 pages Grune & Stratton Inc New York, N Y 1957 Price \$8.75
- PRACTICAL ALLERGY** by M. Coleman Harris M D F A C P and Norman Shure M D F A C P 471 pages illustrated J. A. Davis Co Philadelphia Pa 1957 Price \$7.50
- THE YEAR BOOK OF PEDIATRICS (1957-1958 Year Book Series)** edited by Sydney S. Gellis M D 469 pages illustrated The Year Book Publishers Inc Chicago 11 Ill 1957 Price \$7.50
- RECOVERY FROM SCHIZOPHRENIA The Roland Method** by John F. Davis Sc D 162 pages Charles C Thomas Publisher Springfield, Ill 1957 Price \$4.75
- MICROSCOPIC ANATOMY OF THE TEMPORAL BONE** A Photographic Survey of Serial Sections of the Temporal Bone Cut in the Three Critical Planes of Sectioning Human Specimens by Dorothy Wolff A B M A Ph D Richard J. Bellucci B S M S M D and Andrew A. Pfenner B S M D 414 pages illustrated The Williams & Wilkins Co Baltimore Md 1957 Price \$12.50
- ANATOMY OF PAIN** by A. D. Keele M D F R C P 206 pages illustrated Charles C Thomas Publisher Springfield Ill 1957 Price \$5.50
- ADVANCES IN TUBERCULOSIS RESEARCH** edited by Dr Hans Blekkere (Basel) and Dr Hubert Bloch (Pittsburgh Pa) Volume VIII BCC A Discussion of its Use and Application 316 pages illustrated Charles C Thomas Publisher Springfield Ill 1957 Price \$11
- THE INCURABLE WOUND and Further Narratives of Medical Detection** by Berton Roueche 177 pages Little Brown & Co Boston Mass 1957 Price \$3.50

## UNEXPECTED REACTIONS TO MODERN THERAPEUTICS—ANTIBIOTICS

by L S b d l M D 146 p ge Charles C Th m P b l h  
Sp ngft ld Ill 1957 Pr \$3

## THE DIAGNOSIS AND TREATMENT OF INFECTIONS by D G t j m s

M A M D (C t b) M R C P (L d) 234 p g Charles C Th m  
P b l h Sp gf ld Ill 1957 P \$6

## THE HANDICAPPED AND THEIR REHABILITATION d t d by H ry A

P t t s M D F A C P I t d t by M j G l M f  
J M USMC R (R t) 944 p g ll t t d Ch l C Th m s  
Publ h Sp gf eld Ill 1957 P \$14 75

## AUTONOMIC IMBALANCE d th llyp th l m Impl c t f r Phy l gy

M d c P ych l gy d Ne p y h t y by Ern t G l l b M D  
Ph D 300 p g ill t t d U ty f M t P M  
p l M 1957 P \$8 50

## SHOCK AND CIRCULATORY HOMEOSTASIS T ct o f th F fth Con

f N mb 30 D mb l d 2 1955 P c t N J d t d  
by H ld D G M D D S 337 p ge ll t t d Jo h M y  
J Found t: N w Y k N Y 1957 P \$4 75

## Sym p s m DISEASES AND SURGERY OF THE LENS T s t f

Th N w O le A d my f Ophth lm l gy 1956 ed t d by G g  
M H k M D F A C S d Elt b th M McF t dg M A Art  
Ed t D Al d 260 p g ll t t d Th C V M by C  
St L M 1957 P \$10 50

## PSYCHIATRY AND CATHOLICISM by J m H Vand V ldt P F M

Ph D and R b t P Od w ld M D F A P A 2d ed t on 474  
p g Th Bl k to D i o McGraw-H ll B k C In N w Y k  
N Y 1957 P \$6 25

## JAPAN DICTIONARY J pan l by L w B b 226 p g ill t t d w th

c l d m p d fr t sp Ph l ph l L bary I N w Y k  
N Y 1957 P \$10

## MANUAL OF PEDIATRIC PHYSICAL DIAGNOSIS by L w A B m

M D 195 p ge ll st t d Th Y Book P b l h e I c Chic g  
Ill 1957 Pric \$4

## ATOMIC ENERGY IN MEDICINE by K E H l n Th At m fo P S

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It will be noticed that during the same period the 12 month average strength in all three services has steadily increased. Again part of this increase may be due to those who are in the various residency training programs. So far however about 70 per cent of those in the e programs have signified their intention of remaining in the Regular Service although it is too early to draw a definite conclusion.

BERRY

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Secretary for  
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UNITED STATES ARMED FORCES  
MEDICAL JOURNAL

Volume IX

**March 1958**

### Number 3

## ACUTE RADIATION SYNDROME IN MAN

### Military and Civil Defense Aspects

HERBERT B GERSTNER M D

**I**N AN ADDRESS to the 62d Annual Convention of the Association of Military Surgeons of the United States held in November 1955, Major General James P. Cooney, Deputy Surgeon General of the Army, stated

In the past ten years a great deal of effort has been spent in trying to understand and teach various detailed effects of nuclear weapons. One of the efforts has involved discussions of detailed physics and chemistry relating to the bomb and the microseconds following the explosion. This approach has led to a preoccupation with details that do not help us as medical people to solve the casualty problems. In the preoccupation with these details has resulted in the creation of an aura of mystery around the weapon that has prevented the individual from understanding the things that are essential to his neighbor if they are to survive.<sup>1</sup>

nuclear energy is already producing electricity, pro-  
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factural evidence is frequently clouded by emotional and political considerations. Under these circumstances it is difficult to arrive at an objective and sensible judgment.

The present report restricted to the acute effects of human whole body exposure to penetrating ionizing radiation attempts a realistic evaluation of facts as they are known at this time. Clinical features essential from the standpoint of the practical physician and the medical officer have been emphasized while those of more academic interest have been omitted or treated cursorily. Such an endeavor to present to the practitioner a coherent and unified clinicopathologic concept on which to base his actions necessarily must involve oversimplifications that with increasing information may be subject to revision.

In case of accidental or intentional nuclear explosions an estimate can be made of the air dose of penetrating ionizing radiation to which a group of persons has been exposed. The physician then called into action will face two questions of paramount importance: (1) Is it possible from the air dose to predict the fate of the exposed persons—that is to arrive at a reasonably correct prognosis? (2) Is it conceivable from the air dose to anticipate for a population the degree and the time course of the ensuing disease and thereby to estimate the medical requirements—personnel, hospital beds, and supplies?

#### THE TYPICAL ACUTE RADIATION SYNDROME

Exposure to a sufficient amount of penetrating x ray, gamma, or neutron radiation causes in man characteristic clinical sequelae—the acute radiation syndrome. This complex of signs and symptom, unfolding along a rather fixed time schedule, forms a peculiar picture that is as well defined as lobar pneumonia or typhoid.

or even of exerting strenuous physical effort. This favorable state, the "latent period," may extend to the 19th or 20th post-radiation day, when a new phase is entered rather abruptly. As in the acute onset of an infectious disease, the patient experiences chills, malaise, a feverish feeling, fatigue, and shortness of breath on exertion. Again the general condition deteriorates rapidly and, within 2 or 3 days, hospitalization becomes necessary. Manifestations of severe bone marrow depression—characterized hematologically by leukopenia, thrombocytopenia, and anemia—appear in the form of frank hemorrhages, purpura, susceptibility to infection (especially in the oral cavity), fever, and other signs and symptoms associated with such disorders of the blood picture. This phase of aplastic anemia culminates about the 30th day when the patient passes through a critical state. Thereafter recovery starts and becomes obvious between the 40th and 50th days when fever disappears, infectious lesions in the oral cavity heal, and the blood picture approaches normal values. Convalescence begins after the 60th day and is followed by resumption of work and normal life approximately 3 months postexposure.

According to their chronologic sequence, four distinct stages of the acute radiation syndrome can thus be established—namely, prodromal, latent, bone marrow depression or aplastic anemia, and recovery phases (fig 1).<sup>2</sup> Of course, the "typical" disease, as described above, will be subject to variation and modification brought about essentially by two factors—dose and individual susceptibility. Before these modifications can be discussed, however, a survey must be made of the material on which the analysis is based.

#### ORIGIN OF DATA USED FOR EVALUATION

The largest group of persons exposed to nuclear radiation is represented by the populations of Hiroshima and Nagasaki. Careful and comprehensive clinical<sup>2,3</sup> as well as pathologic<sup>3,4</sup> observations are available. Although these data are outstanding for establishing consequences of human exposure to ionizing radiation, they are of rather limited value for deriving dose-effect relationships, since frequently even a rough estimate of the dose is impossible. Subsequently, reference to the Japanese bomb casualties appears under the abbreviation *JBC*. On 1 March 1954, the test explosion of a hydrogen device at Bikini Atoll accidentally exposed 28 Americans and 239 Marshallese to fallout radiation. Determinations of dose and clinical sequelae are well documented.<sup>5-7</sup> According to the four islands on which these persons were located, four dose groups can be formed that will subsequently be designated as *III*<sub>1</sub> (Utrik), *III*<sub>2</sub> (Ailinginro), *III*<sub>3</sub> (Rongerik), and *III*<sub>4</sub> (Rongelap Atoll). During the same test shot, 23 Japanese

aboard a fishing boat were also exposed to fallout radiation. This group for which dose and clinical sequelae are relatively well known - will subsequently be designated as *JF*.

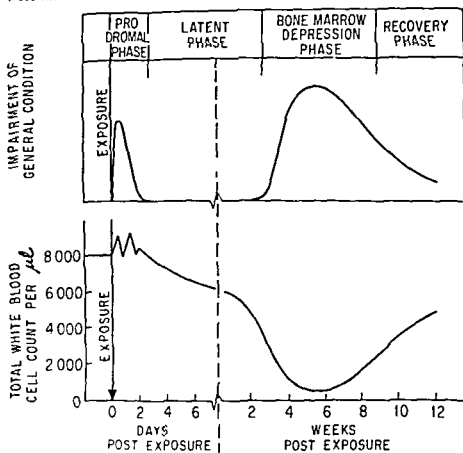


Fig. 1 Schematic drawing showing typical clinical courses of the acute radiation syndrome (hemipneumothorax). The platelet count would parallel the white blood cell count while lymphocyte count would decline and recover.

Two nuclear accidents occurred at the Los Alamos Scientific Laboratory. Uncontrolled fission reactions caused the inadvertent exposure of 10 persons to complex ionizing radiation. Detailed analysis of dose and clinical course are available for 9 of these cases. They will be designated as *LA*. *LA* keeping the indices identical with Hempelmann's numbering of the patients. On 2 June 1957 at the Argonne National Laboratory 4 persons were exposed to neutron and gamma radiations released by the accidental excursion of a water moderated critical assembly. Doses and clinical picture have been well established for each individual patient. These cases will be designated as *A*, *A*, *A*, and *A*. At the Geneva Conference on Peaceful Uses

of Atomic Energy, Guskova et al.<sup>14</sup> reported 2 Russian cases of the acute radiation syndrome as the result of a short gamma and neutron irradiation, after the rules of operating an experimental reactor had been violated. These 2 patients, for whom dose and clinical course are well reported, will be designated as  $R_1$  and  $R_2$ .

Over a long period of time, through radiotherapy a wealth of information about effects of ionizing radiation on man has accumulated. By definition, however, the treatment of the patient will be such that generally only local reactions occur and severe systemic responses will be avoided. In several instances nevertheless, relatively high doses of whole-body x irradiation have been administered as a palliative procedure in advanced and generalized neoplastic disease. European experience with this type of treatment, termed *teleroentgen therapy* was summarized in an optimistic report given by Mallet at the International Cancer Congress at Brussels in 1936. Later publications<sup>15</sup> were more reserved and warned of serious complications that might be encountered in the higher dose range. An interesting method of whole body exposure was developed by Heublein.<sup>16</sup> Several patients, lying in their beds received simultaneously irradiation from a strongly filtered x ray unit at a distance of 5 meters. Exposure lasted through 20 hours of each day and was continued until doses up to 300 r had been accumulated during 1 week; approximately 100 r were delivered. Medinger and Craver<sup>17</sup> reported on 270 patients treated by this technique. To answer some medical questions that arose in connection with the Manhattan Project, the effect of whole body exposure to x rays was studied in several groups of patients undergoing radiotherapy and in one group of 3 healthy volunteers.<sup>18-20</sup> Following introduction of chemotherapy as a palliative procedure in advanced cancer patients whole-body x irradiation was re-examined and its effectiveness compared with that of various cancerocidal substances.<sup>21-22</sup> Unfortunately the above-listed clinical material is of limited value for the present analysis since, predominantly radiotherapeutic effects have been well described, while systemic reactions as related to dose have only occasionally been mentioned. Therefore these clinical groups together will subsequently be considered as a whole. Recently, a detailed study—comprising dosimetry,<sup>23</sup> radiobiologic aspects<sup>2</sup> and therapeutic evaluation<sup>2</sup>—has been reported on 263 cancer patients. These data will subsequently be designated as *MDA*.

Singly each of the above listed sources—bomb casualties, accidental exposures and radiotherapeutic irradiation—are inconclusive because they are compromised by the facts that either the dose and type of irradiation are ill defined (*JBC*) or that whole body exposure to penetrating rays is complicated by simul

taneous superficial effects of alpha and beta radiation ( $^{41}$  and  $^{42}$ ), or that the exposed person is not a healthy human being ( $^{43}$ ). Collectively, however, these data allow reasonable conclusions about the interrelationship between dose and clinical course as shown in the following section.

### DEPENDENCY OF THE ACUTE RADIATION SYNDROME ON AIR DOSE

Analysis of the relationship between dose and clinical effect first requires definition of the two terms. The *air dose* to which a certain person has been exposed is exactly known only in cases of therapeutic application where quality and quantity of ionizing radiation can readily be measured. In all other instances these factors have been derived by estimation, frequently a very difficult problem because of the complex nature of the radiation—ranging through a wide section of the electromagnetic spectrum and containing various amounts of corpuscular components. In these cases, therefore, designation of the air dose in roentgens is subject to a considerable margin of error; however, since a similar degree of uncertainty may exist in future emergency situations, such a crude procedure appears justified. A detailed discussion of the dosimetry problem lies beyond the scope of this report. The severity of radiation-induced clinical sequelae will subsequently be designated as *trivial*, *light*, *moderate*, *serious*, *fatal*, and *lethal*. *Trivial* denotes subtle and very transitory deviations from normal or none at all; *light*, mild signs and symptoms requiring neither medical attention nor treatment; *moderate*, well tolerated radiation syndrome manageable ambulatorily; *serious*, hospitalization necessary, good chance for recovery; *fatal*, poor chance for recovery; *lethal*, no chance for recovery. In the following paragraphs the clinical effects will be discussed as they develop with increasing air dose (tables 1 and 2).

#### Dose range 0-0.1 r

As shown by the corresponding section of table 1, this dose range is generally asymptomatic and, without exception, the clinical course is trivial. Case 4, on the 15th day after exposure, displayed in the right eye, immediately inferior to the limbus of the optic disk, a very small flame-shaped hemorrhage (*a* in table 1) that disappeared one month later. The  $^{41}$  group showed indication of a light depression of leukocytopoiesis (*b*) since lymphocyte and thrombocyte counts were somewhat lower than those of the control, especially around the 29th postexposure day when the maximal effect on the peripheral blood elements must be expected to occur. Case 1 felt nauseated (*c* in table 1) several hours after the accident but ascribed this symptom to nervousness at the accident. Among the  $^{42}$  cases only one patient reported a brief episode of nausea on the day of treatment.

TABLE 1 *Dependency of the acute radiation syndrome on air dose subthreshold range*

Source of information	Number of subjects	Air dose (r)	Physical state	Biological dose (dep. st.)	Exposure time (hr)	Latency (days)	Epithelial changes	Dose rate (r/hr)	Clinical course
<b>Dose range 0-50 r</b>									
A	1	12	-	-	-	-	-	-	T
MI <sub>1</sub>	157	14	-	b	-	-	-	-	T
LA <sub>2</sub>	1	31	-	-	-	-	-	-	T
LA <sub>10</sub>	1	35	-	-	-	-	-	-	T
LA <sub>9</sub>	1	45	-	-	-	-	-	-	T
MDA	188	15-50	-	c	-	-	-	-	I
<b>Dose range 51-100 r</b>									
LA <sub>8</sub>	1	70	-	d	-	-	-	-	T
MI <sub>2</sub>	18	69	-	f	-	-	-	-	T
A <sub>3</sub>	1	70	-	-	-	-	-	-	T
MI <sub>3</sub>	28	78	-	k	-	-	-	-	T
MDA	26	75-100	-	-	-	-	-	-	T
<b>Dose range 101-150 r</b>									
LA <sub>7</sub>	1	145	-	-	-	-	-	-	T
MDA	13	125-150	-	m	-	-	-	-	I L M

T Trivial  
L Light

M Moderate

Low dose selected for explanation

TABLE 2. Deep ocean, 100–1000 m in the Pacific off the west coast of North America, 1977–1980

[illegible]

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while the rest were completely asymptomatic. In connection with the Manhattan Project, 3 healthy volunteers received 21 r of x radiation to the whole body, they showed neither hematologic changes nor any other adverse effect.<sup>18</sup> The same was true in a group of cancer patients, with the exception of a slight decline in lymphocytes occurring rather consistently at doses of 40 r or higher.<sup>19</sup> *In summary, then, it can be stated that the dose range from 0 to 50 r is subthreshold for the acute radiation syndrome and presents no medical problem in emergency situations.* From a purely military standpoint, a recent British publication<sup>20</sup> concludes that at this level no serious disability is to be expected and that the irradiation can be ignored, apart from recording its occurrence.

Although a thorough discussion of possible late effects and genetic consequences of exposure to ionizing radiation does not belong to the objectives of the present report, a few remarks appear appropriate at this time. All evidence, supplied by thousands of patients having received therapeutic doses in this range and by bomb and accident data so far as they can be evaluated today, points to the fact that acute reactions, if existing at all, will completely disappear and that perfect recovery will occur. Shields Warren, in the foreword to reference 12, states "The story of the survivors shows that an individual can be exposed to a large dose of radiation and still return to a productive vigorous life." The concepts of accelerated aging and shortening of life span,<sup>21</sup> as derived from contradictory animal experiments should not be applied to man, at least not in the low dose ranges until they can be founded on strong affirmative observations. Tolerance to additional small amounts of irradiation will practically be normal. In this respect the National Committee on Radiation Protection and Measurement<sup>22</sup> declares "An accidental or emergency dose of 25 rems (roentgen equivalent man) to the whole body, occurring only once in the lifetime of the person, shall be assumed to have no effect on the radiation tolerance status of that person. At the Chalk River Conference (quoted from reference 29) it was agreed that no manifest permanent injury is to be expected for a single exposure of the whole body equivalent to 25 r or less, with a possible exception in the case of pregnant women. Evidently, as far as the exposed individual is concerned, doses up to 50 r do not present clinical problems; however, they may assume significance for future generations if large numbers of the younger population have been irradiated. Animal experiments suggest that doses of 30 to 50 r will probably double the spontaneous mutation rate in man. Since most of the mutations are undesirable, this increased rate may be a real problem for the nation as a whole. However, much more information is required before the size of the potential genetic hazard can be realistically assessed."



## Dose range 51-100 r

As revealed by the corresponding section of table 1 this dose range is subthreshold for the acute radiation syndrome and the clinical sequelae are consistently trivial however a few sporadic individuals with high radiosensitivity show indications of a beginning though clinically insignificant depression of leukocytopoiesis between the 3d and 6th week the lymphocyte count is well below normal while the granulocytes decrease to slightly subnormal values In case LA the total leukocyte count had fluctuated between 5 500 and 8 000 cells per cubic millimeter prior to the accident after exposure it showed a typical initial period of instability (fig 1) and then declined gradually to a minimum of 5 000 around the 20th day (d in table 1) Among the MI population only one member showed mild prodromal symptoms with nausea (e) during the first 2 days postexposure The group means for white blood cells neutrophils and lymphocytes appeared to be slightly subnormal (f) throughout several months while the platelets showed a definite minimum between the 20th and 30th postradiation days From a clinical standpoint however these changes were inconspicuous the maximal depression of the total white count being somewhat below 5 000 in 3 cases only Between the 27th and 42d postexposure days there occurred an epidemic of upper respiratory diseases (g h) which most likely was unrelated to irradiation Epilation and skin injuries (i) definitely were consequences of direct contact with fallout material On the 3d postradiation day case A vomited on several occasions (j) and had four loose stools These effects were believed to be manifestations of anxiety and tension rather than reflections of a true prodromal phase Findings in the MI group (F) essentially paralleled those of the MI population however there was no case with prodromal symptoms and neither epilation nor skin lesions developed because of early decontamination The 26 patients of the MDA series as well as 4 additional cases exposed to 60 r were completely asymptomatic with the exception of a slight decrease in lymphocytes occurring in the latter cases In summary then it can be stated that doses between 51 and 100 r will cause if at all but trivial and transitory clinical changes posing no medical problem According to present day knowledge these mild acute effects are followed by complete recovery and return to normal life Nevertheless additional irradiation should be restricted as much as possible since a lowering of radiation tolerance may persist As to this dose range a British publication<sup>2</sup> concludes approximately as follows Slight, but not incapacitating illness may occur in a number of cases There is no need to break off an important military mission however as soon as convenient, the exposed men should be placed under medical observation for 60 days and symptoms should be treated as they

arise. Afterwards, for about one half year, monthly blood counts should be performed.

#### Dose range 101-150 r

Although, as shown by the corresponding section of table 1, observations are too few to allow a definite statement, the MDA data suggest the following. The acute radiation syndrome, with well developed prodromal and bone marrow depression phases, becomes noticeable in about one third of the exposed persons (1 m). Consistently, however, these changes are so moderate in degree that they can be handled ambulatorily and, therefore, do not pose clinical problems. Three additional patients exposed to 120 r remained asymptomatic.<sup>14</sup> Hence conclusions parallel those given for the previous dose range.

#### Dose range 151-200 r

This most important range is well documented as revealed by the corresponding section in table 2. Dose and clinical course have been established for two relatively large groups—MI and MDA. Since these data represent the best ones known for man, some detailed discussion appears appropriate. The typical acute radiation syndrome evolving in its four phases along a rather fixed time schedule (fig. 1), was clearly noticeable in approximately 70 per cent of the MI group and in 90 per cent of the MDA patients.

Among the MI population about two thirds experienced nausea and one tenth reported vomiting and loose stools. Without therapy these effects had subsided by the 3d postradiation day. The bone marrow depression phase varied in degree from trivial to moderate. In all of the exposed persons both platelet count and total white blood cell count decreased and were at a minimum between the 25th to the 30th and between the 40th to the 45th day, respectively. More revealing from a clinical standpoint, are the following findings. Of the entire population 10 per cent reached platelet values of less than 65 000, 50 per cent attained a white blood cell count of less than 4 000 and 10 per cent fell to a white blood cell count of less than 1 500 per  $\mu$ l. However, even the patients showing the most pronounced depression must still be considered as border line between moderate and serious since they did not develop definite clinical complications and remained physically active. Frank hemorrhages and purpura were absent, blood transfusion was not required. The epidemic of upper respiratory diseases that spread through the Marshall Islands between the 27th and 42d postexposure days (n, o) caused in the group with low leukocyte counts, neither greater incidence nor clinical signs and symptom of greater severity than in the other groups. Therefore, in agreement with radiotherapeutic experience Cronkite et al.<sup>15</sup>

concluded that such degrees of radiation induced bone marrow depression are still well tolerated and that coincidence between epidemic and height of radiation effects was caused probably by chance. Again epilation and skin injuries (*p*) definitely were consequences of direct contact with fallout material.

Among the *MDA* patients 15 per cent remained asymptomatic during the prodromal phase while 35 per cent experienced nausea alone and 50 per cent reported nausea with vomiting. In the majority of instances these complaints could be handled by psychologic reassurance; however 5 cases required additional medication of chlorpromazine hydrochloride and 2 patients were so severely affected as to demand parenteral fluid supply. On the 3d postradiation day the initial reactions had subsided. After a latent period of about 3 weeks the patients entered the bone marrow depression phase ranging in severity from trivial to serious. In a group of 20 patients who could be observed regularly all developed thrombocytopenia with a platelet count of less than 70 000 per  $\mu$ l, reaching the minimum on the 25th day. 8 exhibited leukopenia with fewer than 2 500 white cells per  $\mu$ l, the group mean passing through a minimum on the 32d day and 2 displayed a white blood cell count of fewer than 1 000 per  $\mu$ l. During the bone marrow depression phase complications were as follows: frank hemorrhage was common; it was mostly self limited; however and of little clinical concern; purpura occurred in 4 patients (*q*); and infection developed in 1 case (*r*, *s*). The clinical course of the acute radiation syndrome must be classified as serious in at least 3 of the patients. Here hospitalization and intensive medical treatment with repeated blood transfusions and antibiotics were mandatory.

Under the assumption that air dose specifications for the *MI* and *MDA* groups are comparable (analysis of the problem lies beyond the scope of the present report) and under the assumption that tolerance to penetrating ionizing radiation is not materially different between healthy human beings and advanced cancer patients the following summarizing statements can be made: *In the dose range from 150 to 200 r the acute radiation syndrome becomes noticeable in the majority of an exposed population and it reaches clinical significance in a few highly radiosensitive persons. Approximately 400 r will be the clinical tolerance dose or the threshold dose beyond which an appreciable number of individuals among the exposed population can be expected to develop significant complications requiring hospitalization and intensive medical treatment.* The preceding statement is also supported by additional radiotherapeutic experience<sup>1, 17</sup> indicating that whole-body doses up to 200 r are relatively safe whereas serious complications may occur at higher dose levels.

Present-day knowledge leads to the conclusion that in this dose range, complete recovery will follow after the patient passes through the acute radiation syndrome, even in its more severe forms. Physical fitness and work capacity, when impaired, will have returned to normal values about 3 to 4 months following exposure, while complete restoration of the blood picture may frequently require a much longer period of time (*MI* groups and *JBC*). It is evident that additional irradiation should be kept as low as possible because of a decreased tolerance level.

#### Dose range 201-400 r

In this dose range, as revealed by the corresponding section of table 2, the acute radiation syndrome is fully developed and ranges in severity from moderate to grave. Case *R*, displayed the disease almost in its classical form. A 3 day prodromal phase with general weakness, headache, drowsiness, nausea, and vomiting was followed by a latent phase extending through more than 2 weeks. Abruptly on the 24th postexposure day, the bone marrow depression phase became evident clinically by pronounced general debility, insomnia, fever, petechial bleeding into the skin, frank hemorrhage from the gums and a drop in white blood cell count, reaching a minimum of 780 per  $\mu$ l, at about the 33d day. Infection was absent (*t*) probably because of the early prophylactic administration of antibiotics. Entrance into the recovery phase became conspicuous during the 7th postexposure week. Complete restoration of health and work capacity ensued, as judged by a final medical examination at 1½ years after the accident.

Discussion of the *JF* group seems justified since, here, several important aspects of the acute radiation syndrome are well demonstrated. Early in the morning of 1 March 1954, while the fishermen (17 to 39 years of age) were laying out their nets about 100 miles off Bikini, they saw a faint red light on the westerly horizon, and 7 minutes later they heard a dull noise followed by two sharp explosionlike sounds. Three hours thereafter fleecy clouds appeared and a white substance began to descend from the sky. This fallout continued for 5 hours, and the deck of the boat looked as if it was covered by frost. Within a few hours the crew complained of fatigue, headache, drowsiness, loss of appetite, nausea, and vomiting; they felt so tired that they slept almost continuously except when aroused by other members. All reactions were relatively mild, however, and had completely disappeared by the 4th day. With the exception of minor skin lesions, obviously caused by direct contact with fallout material, the crew was asymptomatic and in good spirits during the entire return voyage that lasted 13 days. On arrival in Japan, 2 men had skin injuries serious enough to require hospitalization; the others went home or remained on the boat. They looked healthy and felt quite well. Within 2 weeks

(4 weeks after start of exposure) however the entire crew and the captain had to be hospitalized because of signs of a progressing bone marrow depression. Fatigue, fever and infection were common, while hemorrhagic diathesis was occasional. Total white blood cell and thrombocyte counts were at the minimum between the 30th and 45th days. At the time of severest depression the white blood cell count fell below 4 000 in all crew members below 3 000 in 18 below 2 000 in 5 and to 1 000 or less in 2 men. Throughout April 4 to 8 weeks after start of exposure the general clinical condition of the fishermen remained serious then improvement became evident. In the majority of cases the blood picture returned to normal rather quickly however in several instances recovery proceeded slowly and encompassed a period of several months. The acute radiation syndrome was complicated by acute hepatitis that appeared in 17 of the 23 fishermen during the middle of May and caused 1 man's death on 23 September 1954 almost 7 months after exposure. That hepatitis had previously caused the death of 2 brothers of the deceased is noteworthy. Although the etiology of this burst of hepatitis in the fishermen remains unsolved the following possibilities are listed in declining order of probability: first serum hepatitis induced by numerous blood transfusions second hepatitis promoted by decreased resistance to infection and third hepatitis due to internal contamination with fission products. Since the fallout material was not evenly distributed over the boat and since the shielding effect of the ship's structures varied at different locations the crew had been exposed to gamma doses probably ranging from 200 to 400 r each person's dose depending on his duties.

The JF group demands particular attention for two reasons: (1) It indicates that 13 day fallout radiation (the dose rate of which declines according to the decay law of fission products) induces the same clinical picture and the same time course of disease as short term exposure. (2) It demonstrates that during the latent phase a crew is able to perform normal work and to accomplish all the tasks necessary for safe return of a boat in spite of the fact that the ensuing bone marrow depression phase proceeds in a serious or even grave clinical course.

*In summary then it can be stated that in the dose range from 200 to 400 r the clinical course of the acute radiation syndrome is predominantly serious or grave. All exposed persons will require hospitalization and intensive medical treatment. However these measures if they can be instigated properly promise a favorable outcome and most likely recovery to a normal and vigorous life. Final judgment on this point must be held in abeyance until follow up studies on the Japanese fishermen are available. The physician's efforts can be expected to be most rewarding in this dose range since here many lives can be saved.*

## Dose range 401 600 r

As shown by the corresponding section in table 2, this range is documented by 3 cases only. Patients  $LA_4$  and  $R_2$  displayed typical pictures of the acute radiation syndrome, while patient  $LA_1$  presented a fulminating clinical course which included gastrointestinal disturbances. A group of 4 hopelessly advanced cancer patients treated with whole body x irradiation by den Hoed et al,<sup>15</sup> most likely, falls also in the upper part of this dose range, an exact classification is impossible owing to the technique and dosimetry employed. Of these patients, 3 died under circumstances indicative of the acute radiation syndrome. At that time, it had not yet been established that the maximal bone marrow depression will occur 4 to 6 weeks postexposure, and it was still considered safe to continue whole body irradiation, with intervals of only a few days between each exposure, as long as the leukocyte count did not fall below 2,500 per  $\mu$ l. Thus the authors were completely surprised when about 3 weeks posttreatment granulocytes disappeared "almost completely," thrombocytes were hardly present, hemorrhage from gum and nose appeared, and petechial bleeding in the skin became evident. Moreover, fever and infection complicated this picture of "agranulocytosis" and caused death of the patients between 3 and 7 weeks after cessation of radiotherapy. In addition much of the *JBC* data can be assumed to fall in this dose range; there exist also numerous animal experiments that allow cautious extrapolation.

When all the direct and indirect evidence is taken into account, the following inference may be made. Up to about 500 r, the clinical course of the acute radiation syndrome is largely determined by radiation effects on the lymphoid tissue and the bone marrow—the most radiosensitive cell groups of the adult individual. Temporary depression of the gonads need not be considered in this regard since no serious constitutional reactions are involved. At doses above 500 r, however, direct radiation damage to the epithelium of the gastrointestinal mucosa—the next cell group in radio sensitivity—becomes a decisive factor. In the generative centers of the jejunal and iliac crypts, particularly, radiation causes arrest of mitotic activity. This production block of viable new cells, combined with decay of already existing cells, leads to denudation of the intestinal wall.<sup>16</sup> Functionally, the structural change has several serious consequences. As shown by Brecher and Cronkite,<sup>17</sup> water and electrolyte loss into the lumen of the alimentary tract may be so severe as to cause vascular collapse. Furthermore, denudation of the mucosa together with a defense mechanism weakened by bone marrow depression, leaves the organism wide open to invasion by toxic substances and bacteria. These factors singly or combined, are responsible for the fulminating clinical course of the disease. In the fulminating forms a clear

latent phase is no longer present and death may occur at any time during the first 3 weeks postexposure while patients showing predominantly hematopoietic depression succumb if at all during the critical period extending from 3 to 6 weeks postirradiation<sup>2</sup>

*In summary then it can be stated that in the dose range from 400 to 600 r the clinical course of the acute radiation syndrome is predominantly grave. Up to 500 r the bone marrow injury still determines clinical picture and outcome whereas at higher doses direct damage to the epithelium of the gastrointestinal tract becomes more and more the decisive factor bringing about a fulminating course of the disease—the gastrointestinal form of the acute radiation syndrome.*

The gastrointestinal form of the acute radiation syndrome is illustrated by one of the nuclear accidents LA. The scientist involved was performing critical mass determinations. For that purpose two pieces of bomb material hemispheres the size of a split baseball mounted on a rack were slowly pushed toward each other. Neutrons from an outside source triggered in the fissionable material chain reactions that became more intense with narrowing air gap. Just before reaching the critical distance—and thus before an explosive build up of chain reactions occurred—the hemispheres had to be separated. One day the bomb materials accidentally came too close together and the reaction in the critical assembly began to run away emitting massive amounts of penetrating ionizing rays. The scientist was exposed to a combined neutron gamma and roentgen radiation of about 2 000 r to the whole body. He experienced nausea within a few minutes and he vomited before reaching the hospital about 60 minutes later. During the next few hours vomiting increased in frequency and one loose diarrheal stool was passed. From 12 hours post-exposure onward these prodromal reactions ceased completely and the general condition began to improve. The patient remained in satisfactory condition until the 6th day when a grave deterioration took place abruptly. The white blood cell count fell precipitously to very low values the low grade fever existing since the day of the accident rose suddenly above 102 F nausea vomiting and diarrhea reappeared and signs of a severe paralytic ileus developed. The patient's major complaint was abdominal distention. No peristaltic sounds could be heard. By gastric suction 10 liters of a green fluid with fecal odor and appearance were aspirated within a 24 hour period. In spite of continuous gastric suction parenteral fluid supply blood transfusions and antibiotic treatment the deterioration progressed swiftly to beginning circulatory collapse on the 8th day and death on the 9th post exposure day. At autopsy the most striking changes were found in the small intestine. It was distended flabby and filled with

dark brown semiliquid material. The vessels were intensely congested, and there were numerous petechial hemorrhages on the serosal surface. The mucosal surface was edematous and deep red, particularly in the region of the jejunum where, in addition, the surface was covered with a membranous gray green exudate that could be stripped off in sheets.<sup>12</sup> Histologic examination showed complete erosion of the jejunal and iliac epithelium with loss of the superficial submucosal layers. The denuded surfaces were covered by exudate containing masses of bacteria that, in the ulcerated portions, had invaded the intestinal wall. In essence, the anatomic diagnosis was then as follows: Diffuse membranous and ulcerative enterocolitis associated with aplasia and depletion of bone marrow, lymph nodes, and lymphatic system in spleen and gastrointestinal tract.

### HIROSHIMA AND NAGASAKI

At 0815 hours on 6 August 1945 an atomic bomb was detonated approximately 2,000 feet above the city of Hiroshima, and 3 days later at 1102 hours another one was exploded over the city of Nagasaki under essentially the same conditions. Most of the population were either on the streets or in their rather lightly constructed homes and business establishments. In Hiroshima 70,000 to 80,000 persons died, and at least as many were injured. Since 72 of the 190 medical doctors residing in the city perished, and since most of the hospitals were destroyed, catastrophic conditions ensued with respect to care and treatment of the injured.<sup>1</sup> It is understandable that during the first week only the most critically injured patients could be retained and observed closely in the improvised clinical facilities. Most of these casualties, showing combinations of mechanical wounds, thermal burns, and radiation injury, succumbed rapidly.<sup>2, 3, 4, 5</sup> Perhaps one seventh of the total number of injured persons escaped both mechanical lesions and burns, but received radiation doses sufficient to cause clinically significant sequelae.<sup>6</sup> These patients entered medical care in two waves. The first one, comprising predominantly persons exposed at a distance of less than 1,000 meters from the hypocenter, began to appear within a few days after the attack; its start merged with the influx of the numerous casualties showing combined injuries. In this first wave, severe gastrointestinal disturbances—tenacious anorexia, vomiting, and diarrhea associated with extreme weakness—were most conspicuous, predominating the entire clinical course. At the end of the first postattack week, serious leukopenia had developed in the patients still living and was complicated by high fever as well as profuse bleeding in almost every organ. Purpura, bloody diarrhea, bleeding from the gum, epistaxis, hematemesis, and hemoptysis, in this order of frequency, were the most common forms of blood loss.<sup>7, 8, 9</sup> In one group of autopsies, subarachnoid hemorrhage was seen in



60 per cent of the cases. The first wave of casualties had very poor prognosis; the clinical course was fulminating; practically all of these patients died within 2 weeks postexposure from dehydration with vascular collapse or fatal bleeding or septicemia.

The second wave of radiation casualties entered medical care about 3 to 4 weeks after the attack. Since by that time the worst confusion had subsided and the improvised clinical facilities had been much improved and since the Japanese medical personnel had begun to understand the etiology of the unfamiliar disease, clinical observations, laboratory examinations, and hospital records obtained on these patients as compared to those on patients of the first wave were much more complete and reliable. Generally exposure had occurred in open air or in Japanese type housing at a distance of 1 000 to 2 000 meters from the hypocenter; in the occasional instances where the distance had been less than 1 000 meters the individuals had been sheltered by heavy concrete buildings. This second wave of casualties displayed the typical acute radiation syndrome. A brief prodromal phase of 3 days duration was followed by a latent period lasting about 3 weeks. During that time most of the patients continued to work frequently; they participated in the strenuous duties of clearing the rubbish of the city. In only a few instances was there a record of persisting weakness and easy fatigability. Approximately 2 weeks after the attack the hair of the scalp became loose; this was considered an ominous sign. A few days later general malaise, fever, purpura, and other typical complications compelled the patient to seek hospital admission. Hachiva, director of the Hiroshima Communication Hospital, describes in his diary the following case as characteristic. The 28 year old female patient had been inside a solid building at 700 meters from the hypocenter. Shortly after the bombing she developed weakness, nausea, vomiting, general malaise, and diarrhea. Two days later these complaints had vanished and physical strength as well as appetite began to return. Thereafter she ate plenty and did light work although some fatigue and malaise persisted. On the 19th day while combing she noticed large amounts of loose hair. Recognizing this as a portentous sign she asked for a physical examination on the 22d day. Nothing abnormal was found with the exception of severe weakness, epilation of about two thirds of the scalp area, and marked leukopenia. She was admitted to the hospital where her condition deteriorated swiftly. In days postattack the sequence of events was as follows: 25th petechiae and severe malaise; 29th anorexia, increase in size and number of petechiae and fever of 101.5; 33d weak pulse and further enhancement of petechial bleeding; 37th death.

Survey of the entire JBC data revealed a rather uniform clinical course for patients of the second wave. Around

the 20th day after the bombing, general malaise, pharyngeal pain, and ascending unremitting fever appeared. Within a few days, petechiae and ulcerative lesions of lips, mouth, and pharynx became manifest. Leukopenia and thrombocytopenia were most pronounced between the 3d and 5th week postexposure. During this period, representing clinically the critical phase of the illness, severe hemorrhage and overwhelming respiratory or enteric infection caused the death of about 50 per cent of the patients. In the survivors, recovery was heralded between the 5th and 6th week by cessation of the pharyngitis followed by disappearance of petechiae and fever, and finally by healing of the ulcerative lesions. This improvement was associated with an increase in circulating leukocytes and platelets, while red cell count and hemoglobin content of the blood generally continued to decline, reaching the minimum around the 6th and 8th week. Most patients became completely asymptomatic at 3 months following the attack.

Comparison of the *JBC* data with the experience gained from radiotherapy and nuclear accidents leads to several important conclusions. The first wave of casualties obviously represents the fulminating form of the acute radiation syndrome with direct radiation damage to the gastrointestinal epithelium as the determining pathogenic factor. It then follows that these patients must have been exposed to air doses in excess of 500 r. The second wave of casualties evidently represents the typical form of the acute radiation syndrome with hematopoietic depression as the determining pathogenic factor. These patients, therefore, must be assumed to have been exposed to air doses ranging from 200 to 500 r. These conclusions compelling as far as the clinical symptomatology is concerned do not agree with dose estimates calculated from physical considerations. These calculations do yield doses higher than 500 r for the area described around the hypocenter by a radius of 1 000 meters, but they arrive at only 15 r for a distance of 2 000 meters where the clinical picture demands at least 200 r. This obvious discrepancy between medical and physical dose estimates has already attracted attention and speculation about its cause.<sup>9</sup> In the present report precluding the treatment of technical dosimetric problems, this interesting phenomenon cannot be analyzed. The physical factors involved have been re examined in a recent study of the bomb data.<sup>10</sup>

#### SUMMARY OF DOSE EFFECT RELATIONSHIP AND DEFINITION OF CLINICAL THRESHOLD OR HOSPITALIZATION DOSE IN MAN

When for a large group of whole-body irradiated animals the mean survival time is plotted as a function of dose, the graph does not proceed in a smooth curve but forms three distinct steps.<sup>2</sup> Furthermore, it can be shown that these steps reflect three different pathogenic mechanisms. Death is caused, in the

low dose range by hematopoietic depression in the middle dose range by gastrointestinal denudation and inflammation and in the high dose range by failure of the central nervous system. Although the corresponding data are largely unknown for man they can be extrapolated with reasonable accuracy from clinical findings and animal observations. Because of the close agreement of radiation induced effects among the various species of the mammalian class man can be expected to show the three step survivaltime curve depicted in figure 2. Correspondingly three different types of clinical pictures should exist and the

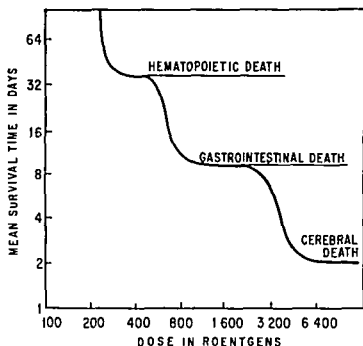


Fig. 2. Mean survival time for a large group of patients extrapolated from clinical data and animal experiments.

acute radiation syndrome should be subdivided as shown in table 3 into hematopoietic, gastrointestinal, and cerebral forms. In man the hematopoietic form of the disease is rather well established—based on a sufficient number of careful observations the gastrointestinal form is but vaguely understood since only two nuclear accidents fall in this range and since JBC records of early cases are not complete and the cerebral form is completely unknown because (1) persons of the JBC group who were close enough to the hypocenter to receive such high doses necessarily experienced also lethal thermal burns or mechanical injuries and (2) patients of this group were lost

during the confusion of the first 3 days postattack without examination and recording

TABLE 3 *The acute radiation syndrome*

	Cerebral form	Gastrointestinal form	Hematopoietic form
Threshold dose	2 000 r	500 r	100 r
Characteristic signs and symptoms	Convulsions tremor ataxia lethargy	Diarrhea fever disturbance of electrolyte balance	Leukopenia purpura hemorrhage infection
Time of death	Within 2 days	Within 2 weeks	Within 2 months

For the sake of completeness (the hematopoietic and the gastrointestinal forms having been treated earlier), an attempt must now be made to predict and describe for man the cerebral form of the disease as it emerges from animal experiments. Weakness, drowsiness, and listlessness—components of the prodromal complex already at low level irradiation—will develop within 1 hour after exposure and will proceed swiftly to severe apathy, prostration, and lethargy. Over this progressive loss of physical and mental activity is superimposed, particularly during the first 3 hours postexposure and at doses in excess of 5,000 r, a disturbance of the motor system. In short intervals seizures will occur either in form of generalized muscle tremor, or ataxic movements, or full blown epileptoid convulsions of the grand mal type.<sup>3</sup> Patients who survive the convulsive phase will be prostrate and somnolent and will expire within 2 or 3 days postexposure. The anatomic substrate for the progressive loss of physical and mental activity must probably be sought in widespread inflammatory foci that begin to develop within 1 hour after irradiation. These nonbacterial radiation induced reactions form the pictures of meningitis, encephalitis, and vasculitis and are soon associated with brain edema. The convulsive seizures, on the other hand, are most likely related to pyknosis occurring in the granule cell layer of the cerebellum within 2 hours postexposure.<sup>31, 3</sup>

Obviously the three characteristic forms of the acute radiation syndrome will be separated from each other by broad dose ranges of transition where mixed effects will result. These more complex clinical pictures, however, become explainable when the pure forms are understood clearly. From a practical medical standpoint it should be reiterated that, so far, the pure hemato-

poietic form and clinical pictures representing a transition from the hematopoietic toward the gastrointestinal form have predominantly been encountered in bomb explosions and nuclear accidents. For future disasters it may be assumed that these forms again will represent the major medical problem. The ensuing sections will therefore be restricted to further analysis of these pictures only.

Ionizing radiation as many other physical and chemical factors brought about or intensified by modern civilization is supposed to be biologically harmful regardless of dose. Obviously it is only a matter of time until there exist laboratory methods refined enough to detect the minute functional changes possibly induced by very low doses. Such alterations unless usable as biologic dosimeters have no bearing on the casualty problem. All negligible are the minor systemic reactions occurring in the low dose range. What really matters is the threshold dose beyond which the clinical course is such that hospitalization becomes necessary for an appreciable number of persons among a large irradiated group. When a military installation or a city has been exposed to a known air dose the medical countermeasures for a dose beneath the hospitalization threshold will be different from the one above it. In the first case psychologic reassurance and taking white blood cell counts as a precautionary measure may be the only things required. In the second case elaborate steps can be taken to prepare beds and medical supplies for the anticipated number of casualties since owing to its relatively long latent phase the actual disease will start several weeks postexposure. Therefore good organization and logistics may be of primary importance. From the previous analysis of data—showing that the hospitalization threshold lies near an air dose of 200 r—figure 3 was designed for typical cases exposed to various amounts of radiation.

#### RELATIVE IRRELEVANCE OF TYPE OF PENETRATING IONIZING RADIATION FOR THE CAUSATION OF THE ACUTE RADIATION SYNDROME

To the medical officer the physical aspects of the radiation problem appear at first glance to be of embarrassing complexity. Biologic injury may be inflicted by high speed particles the various types of which are steadily increasing with progressing knowledge of the nuclear structure and it may also be induced by high energy photons covering the electromagnetic wave spectrum from ultraviolet to the hardest gamma radiation. Moreover a specified amount of radiant energy may be transferred to the organism within seconds as in exposure to the atomic bomb or it may be transmitted over a period of time measured in days, weeks or even years as in exposure to fallout from the hydrogen

bomb. Finally, the radiation source may be located at various distances from the subject or it may be attached to the skin as in fallout contamination, or it may have its seat in internal organs as a consequence of ingestion or inhalation of radio-

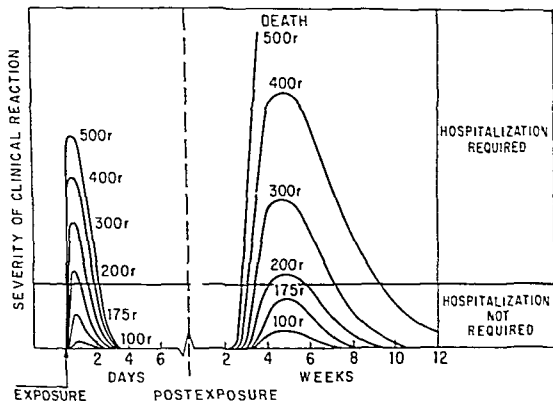


Figure 3 Clinical course of the acute radiation syndrome in typical cases exposed to various amounts of penetrating ionizing radiation. The horizontal line indicates the hospitalization threshold.

active substances. From a practical medical standpoint fortunately, this complexity can be reduced to but a few realistic situations. Although one case of suicide with large amounts of thorium X proves that the typical acute radiation syndrome can be elicited by the uptake of radioactive substances,<sup>4</sup> present day experience indicates that internal irradiation from fallout material is much too small to trigger the acute radiation syndrome or to influence its course.<sup>22</sup> External irradiation, when composed of soft roentgen, alpha, or beta rays, will be absorbed predominantly in the skin and will produce in this organ inflammatory reactions frequently progressing to ulcerative lesions. This disease—the acute radiation dermatitis—has been excellently described as a consequence of fallout contact<sup>7</sup> but it cannot be covered in the present report. External irradiation when composed of hard roentgen, gamma, neutron, or other penetrating rays will cause the acute radiation syndrome. The severity of the clinical reaction is essentially the same regardless of whether a certain dose is delivered within a microsecond

over a period of 4 days an estimate shows that in the latter case the biologic efficiency is decreased by less than 6 per cent. When the time of exposure is extended beyond 4 days however the air dose necessary to cause the acute radiation syndrome increases appreciably with length of exposure time. Therefore to avoid drastic systemic reactions radiotherapy applies fractionated doses each partial dose being separated from the next one by an interval of several weeks. Observations on patients treated with the Heublein technic also demonstrate that the clinical tolerance threshold drifts to higher dose levels for protracted exposure as compared to one of less than 4 days duration. Craver reached the conclusion that advanced cancer patients withstand up to 300 r total body exposure when given over a period from 20 to 30 days and that the lack of systemic effects other than those caused by the progressing disease indicates that such doses may be well tolerated by healthy persons. A dose of 300 r given in one continuous course for 10 days produces definite responses and is about the highest whole body exposure that can safely be administered. When the constitutional reactions in the latter patients are compared with those of the MDA series it appears that 300 r given during a period of 10 days correspond approximately to 200 r applied in 51 minutes. Evidently this shift in threshold necessitates for long term exposures that the accumulated air dose be multiplied by a factor smaller than unity to obtain the effective dose from which prognosis of the expected biologic consequences can be made however exact size and time function of the factor are still unknown for man. Large scale comparative studies with the Heublein technic and the MDA procedure should enable determination of these elements so important in the case where a population is forced to occupy permanently an area contaminated with fallout under which condition there is a marked difference between air dose and effective dose. When people as the JF group have to stay no longer than 2 weeks in the contaminated environment the discrepancy between the 2 doses is less striking and the correction factor deviates but slightly from unity. Calculation based on the decay law for fission products shows that during the first 4 days more than 75 per cent of the total dose emitted throughout the 2 week period has been received. If evacuation can be effected within 4 days after the beginning of fallout as in the WJ groups the uncorrected air dose can be considered as the effective dose. *In summary then it can be stated that all types of penetrating ionizing radiation, singly or combined produce one specific clinical picture—the acute radiation syndrome for exposure times extending beyond 4 days the biologically effective dose will be smaller than the measured air dose*

To emphasize the validity of the previous statement, two sets of data will be discussed—namely, hematology and case histories of a few representative practical examples. In figure 4, the time course of the white blood count is depicted for four different situations involving penetrating ionizing radiation

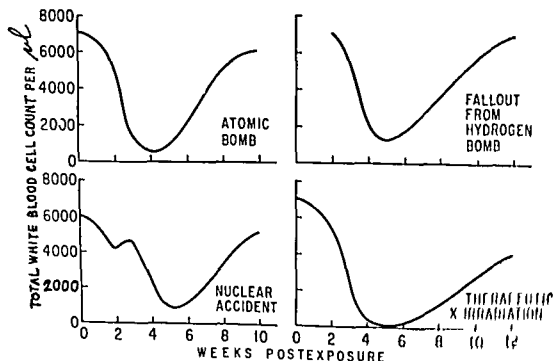


Figure 4 Similarity of the leukocyte response in persons exposed to the types of penetrating ionizing radiation. Origin of data as explained in text.

The origin of the individual curves is as follows: a group of Hiroshima casualties,<sup>17</sup> the atomic bomb, one Japanese fisherman—case B,<sup>18</sup> nuclear accident, case R,<sup>19</sup> and thorium patient 34. Comparison of the curves reveals that in all instances the minima occur between 4 and 6 weeks postexposure. The transitory recovery, in the case of the nuclear accident between weeks 2 and 3, is not a special case because it is seen quite often in response to various types of penetrating ionizing radiation. For clarity, lymphocyte, thrombocyte, and platelet counts have been omitted from figure 4. When lymphocyte count is depressed, the lymphocyte count drops more abruptly, and its recovery is more rapid. The neutrophil count presents a time course similar to that of the total blood cell count while the erythrocyte count recovers more slowly and reaches its pre-exposure level. In the four circumstances depicted in figure 4, the agents are a mixture of gamma photons and



explosion and the nuclear accident gamma photons of various penetrating powers combined with alpha and beta components causing radiation dermatitis for the fallout case and x rays for the therapeutic exposure Yet in spite of this diversity the biologic changes are surprisingly uniform Thus, figure 4 underlines once more the fact that the hematologic response is the same regardless of the type of radiation by which it is elicited Apparently ionizing radiation triggers in the hematopoietic tissues a process that then proceeds according to inherent properties of that biologic system This uniformity of response is even more accentuated by the following excerpts from a few typical case histories

At m b mb d at (JBC) At the time of the Hiroshima explosion a 25 year old older was on the upper floor of a two-story Japanese building located about 1 000 meters from the hypocenter but he was able to leave the city for shelter in the fields On the day after the attack although experiencing malaise he returned to his garrison On the 4th day he resumed his normal duties involving strenuous exercises on the drill field and a 10-mile march Even though epilation noticeable from the 14th day onward indicated serious exposure he continued work until the 21st day when chills a feverish feeling and weakness appeared Petechiae developed 24 hours later and hospitalization became necessary on the 24th day On admission he complained of headache malaise and pain in the oral cavity Beginning with the 26th post attack day pharyngitis with high fever dominated the clinical picture moreover there was swelling of the gingiva superficial ulcerations around the angles of the mouth and dysphagia After the fever had subsided on the 39th day petechiae as well as inflammatory reactions began to appear and he was discharged on the 60th day after the explosion when his white blood cell count had risen to 1400 from a low of 900 per  $\mu$ l Following release from the hospital he resumed work on his own farm

N I ident (R) A 21 year old male patient accidentally received 450 whole-body gamma and neutron irradiation from an experimental reactor when rules of operation were violated Within a few minutes after exposure pronounced weakness headache and vertigo developed and were swiftly followed by an exanthema and vomiting This burst of initial reactions reaching a maximum during the first 24 hours lasted 3 days Thereafter the general condition of the patient improved markedly and remained satisfactory until the 19th day when rather abruptly deterioration began Recurrent chills accompanied by shivering high fever retropharyngeal petechiae and frank hemorrhage from the gums appeared and were soon followed by an extensive ulcerative lesion on compressing the right tonsil This very grave clinical picture persisted throughout a period of 2 weeks then recovery became noticeable Fever disappeared on the 35th postexposure day and petechiae inflammatory reactions and frank bleeding had ceased by the 41st day

The total white blood cell count having been at a minimum of 150 per  $\mu$ l on the 28th day returned to almost normal values. At the end of the 3d postexposure month the patient was released from the hospital and following a 4 week vacation he was able to resume his normal duties.

**Therapeutic x irradiation (MDA, patient 34)** This 55 year old male patient had Hodgkin's disease with lesions in lungs, ilium, 12th rib and 12th thoracic vertebra. Since several courses of limited field roentgen therapy yielded only temporary amelioration, whole-body exposure to a nominal air dose of 200 r was administered in one session. Shortly after completion of the treatment the patient experienced severe nausea, vomiting and extreme weakness necessitating antiemetic therapy with 25 mg doses of chlorpromazine hydrochloride at 6-hour intervals. Even under this medication he vomited 7 times on the day of irradiation and 4 times the following day; thereafter he became asymptomatic with the exception of light nausea on the 3d postradiation day. This favorable condition persisted for 3 weeks. On the 24th postradiation day low grade fever and profound pancytopenia began to develop. Soon multiple gluteal abscesses as well as ulcerating lesions involving gingiva and hard palate appeared and progressed in spite of treatment with penicillin, streptomycin and tetracycline hydrochloride (Achromycin®). Finally, after beta hemolytic *Micrococcus pyogenes* (var. *aureus*) resistant to tetracycline hydrochloride had been found on culture, improvement took place under administration of erythromycin. The patient became afebrile on the 51st day postradiation; soon thereafter the infectious lesions began to heal and the leukocyte count rose to 2,300 from a previous minimum of 100 per  $\mu$ l.

**Fallout from the mononuclear device** (history of a clinically subthreshold case) This 26-year-old mother of four children, a native of the Rongelap Atoll, was exposed to about 175 r of penetrating fallout radiation as an aftermath of the thermonuclear test explosion at Bikini on 1 March 1954.

Approximately 4 to 5 hours after the explosion a white material of snowlike appearance fell upon the island located 120 miles from Bikini. The natives, not aware of the significance of these "snow flakes" that continued to fall for about 1 hour, carried on their every day life in the lightly constructed palm houses and out of doors. At 50 hours after the explosion evacuation was executed by air and surface transportation to the Kwajalein Naval Station. Here clothes were removed and laundered while skin and hair were washed repeatedly with fresh water and soap.

On the day following the fallout this particular patient was nauseated but did not vomit; she also experienced itching and burning of the skin, presumably caused by direct contact with fallout material. These complaints soon disappeared and at the time of evacuation, 2 days after the beginning of exposure, she was feeling well. This favorable general condition, interrupted by a brief episode of upper respiratory infection, persisted throughout the entire observation time of 3 months.

during which period she gained 2 pounds in weight. At several follow-up examinations covering 3 years to the present time no diseases other than occasional cold were reported and no complaints interpretable as radiation effects were disclosed. She has had two additional pregnancies that were uncomplicated and led to the birth of two healthy babies at full term. Since the first of these children was born in January 1955, conception must have occurred in April 1954, that means between 1 and 2 months postexposure. The hematologic findings on this patient (compiled in table 4) show a pronounced minimum of platelets around days 26 and 30 while a corresponding sharp dip of the white blood cell count probably was obscured by the intercurrent infection of the upper respiratory tract.

TABLE 4

*Effect of exposure to penetrating fallout radiation on white blood cell and platelet counts of a 26 year old female native of Rongelap Atoll*

Day following exposure	Total WBC 1 000/ $\mu$ l	Neutrophilic percentage of total WBC	Lymphocyte percentage of total WBC	Platelet 1 000/ $\mu$ l
9	6.2	57	35	150
12	5.2	65	24	—
15	5.9	71	23	160
18	5.8	65	33	105
22	6.8	57	40	120
26	3.3	59	29	60
30	10.0	64	32	50
33	5.7	54	38	130
39	5.9	76	22	160
43	4.1	50	48	240
47	4.5	62	36	180
51	3.8	46	50	135
54	3.0	49	51	120
62	6.9	—	—	160
2 years	9.0	63	34	188

Upper respiratory infection

This case history is of particular interest because it demonstrates that a dose close to the clinical threshold may cause nausea followed by definite hematologic alterations whereas general condition, feeling of well being, physical activity and capability to be trained are not affected.

ROLE OF PENETRATING IONIZING RADIATION  
AS A CASUALTY CAUSING AGENT

Although the atomic explosions over Japan may have had revolutionary impact on military and political planning, their influence on medical concepts was far less striking. In many respects, the problems posed by the great number of casualties were not essentially different from those observed after large scale bombing raids with conventional explosives. Ionizing radiation was a minor complication; heat and blast were really devastating. From a military medical standpoint, therefore, atomic bombs could be conceived as huge conventional bombs with some unusual side effects. It was the explosion of the first hydrogen bomb at Bikini in 1954 that revolutionized medical thinking. The aftermath of this event can still be felt, and its full meaning must be recognized by everybody concerned with medical problems under catastrophic conditions. Emphasized by the accidental exposure of the Marshall Island population and the Japanese fishermen, the Bikini explosion demonstrated that ionizing radiation can become *the* casualty causing agent. Fallout from the bomb may cover thousands of square miles and deposit radioactive material of sufficient activity to be supra threshold for the acute radiation syndrome. This means that a military installation or a city situated hundreds of miles away from a hydrogen bomb explosion will experience neither thermal nor blast effects, and may not even have knowledge of the disaster.

Yet, owing to the prevailing meteorologic conditions, several hours after the explosion, fallout may descend upon the area and expose its population to high amounts of penetrating ionizing radiation. Quite in contrast to Hiroshima and Nagasaki the medical practitioner would then face a type of mass casualty completely different from that seen after conventional bomb attacks, and the countermeasures would have to deviate correspondingly.

Although the fallout problem has been thrust into medical and public attention by the first hydrogen bomb explosion, it should be pointed out that the phenomenon is not necessarily characteristic of this type of weapon (in the present report the popular term "hydrogen bomb" has been used as a synonym for the more general designation "thermonuclear bomb"). The difference between atomic and hydrogen bomb, in this respect, is one of degree rather than of kind. Furthermore the amount of fallout depends strongly on the physical conditions under which a nuclear explosion occurs. Two extreme possibilities will be considered. First, the bomb explodes at a relatively high altitude above ground. In the process of detonation, a large amount of

neutron and gamma radiation is released and transmitted to the earth below. At ground level the intensity of this initial nuclear radiation emitted within the first minute will be determined essentially by the inverse square law and the absorption in air. At the point of explosion a temperature of several million degrees exists and vaporizes the highly radioactive fission products as well as the unsplit fissionable material casing and other parts of the weapon. These hot gases form a highly luminous sphere—the "fireball"—that quickly expands to a diameter of about 200 feet for the atomic bomb and to 8 000 feet for the hydrogen bomb. As the fireball (rising with a rate of roughly 250 to 350 feet per second) cools the vapors condense and the highly radioactive bomb debris is dispersed in the upper layers of the troposphere. The fine radioactive particles are then carried over appreciable distances and slowly descend to earth. Because of its considerable dispersion and late descent this worldwide fallout conveys only minute amounts of radioactive material to the unit of surface area and the thereby emitted residual nuclear radiation is much too small to cause acute biologic effects. The conditions just described existed at Hiroshima and Nagasaki; therefore radiation injuries were caused by the initial nuclear radiation, while residual nuclear radiation was negligible.

Quite a different situation prevails when the explosion occurs at such a low altitude that the expanding fireball touches ground. By its million degree temperature rock, soil and other material are vaporized and added to the above described components. It has been estimated that 20 000 tons of surface substance may thus be vaporized and incorporated in the fireball of a thermonuclear bomb; the amount is less in case of an atomic bomb. Under the intense neutron irradiation during detonation all of this material becomes radioactive. In addition the rising fireball causes high winds at the earth's surface and thereby sucks up additional dirt and dust. As the terrific updraft started by the rising fireball subsides the radioactive particles and contaminated soil material begin to fall gradually back to earth; the heaviest fragments touch ground close to the explosion site, the fine dust falls out later and farther away. This highly radioactive local fallout covering in the Bikini explosion 7 000 square miles causes such a large amount of residual nuclear radiation that as demonstrated by the several accidents it may well be suprathreshold for the acute radiation syndrome and therefore may become one of the most devastating casualty causing agents.

#### VARIATION OF THE ACUTE RADIATION SYNDROME WITH INDIVIDUAL SUSCEPTIBILITY

Individual sensitivity to ionizing radiation varies markedly. Although exact figures are not available a reasonably correct

estimate can be obtained and extrapolated from the *MDA* series, the *MI* population, and several groups of Hiroshima workmen<sup>3</sup> since in these instances large numbers of persons were exposed under almost identical conditions. These data lead to the impression that the extremes in susceptibility differ approximately by a factor of 2, for example, among a large group exposed to 200 r, the most radiosensitive person will develop a clinical picture of the same severity as that exhibited by the most radio-resistant person among a group exposed to 400 r. Or, 300 r may be expected to be lethal to the most radiosensitive individuals, while about 600 r may be assumed to be the border line beyond which even the most radioresistant individual cannot be expected to survive. The reason for this wide difference in radiosensitivity, existing also among laboratory animals, is unknown; age, sex, state of nutrition, and many other factors have been studied in animal experiments without supplying an explanation. When for a large series of identically exposed persons the distribution curve is drawn with respect to clinical course—or more objectively to degree of white blood cell depression—a bell shaped pattern is obtained, as suggested by the above mentioned groups. With increasing dose, this curve will move toward a more severe clinical course (fig 5) or lower white blood cell value. In figure 5, the  $LD_{50}$  for man has been supposed to be 600 r, consistent with most literature reports. Although this value appears to be a reasonable assumption, it should be emphasized that there

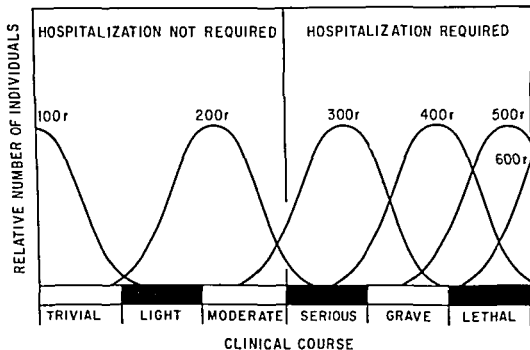


Figure 5 Effect of various amounts of penetrating ionizing radiation on the distribution curve with respect to clinical course. Data for human populations have been derived and extrapolated from clinical observations and animal experiments.

exist no human data establishing the border line for survival definitely at 600 r. When in figure 5 the area is determined between abscissa axis and that section of each dose curve which corresponds to a certain degree of clinical course and when the ratio is calculated for this area to that of the corresponding entire distribution curve a separation of casualties in per cent of their total number is obtained for each dose as shown in figure 6. The heavy horizontal line through the middle of figure 6 represents the *hospitalization threshold*. It must be underlined

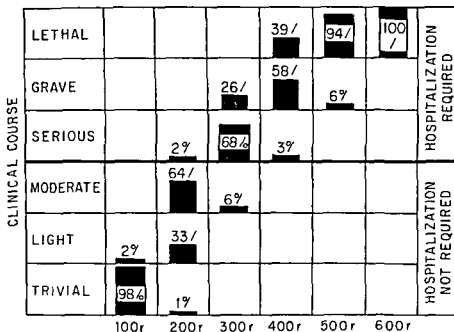


Figure 6. Estimated casualty distribution for various dose penetrations. The data derived from figure 5.

that this threshold according to all human data available is rather sharply defined. Moderate bone marrow depression is surprisingly well tolerated and apparently is associated with no complication other than an increased fatigability. In sharp contrast serious bone marrow depression leads after the latent phase to the sudden onset of the fully developed hematopoietic form of the acute radiation syndrome, requiring immediate medical attention. Figure 6 yields the following information. Suppose a large population has been exposed to an air dose of 300 r. Logically this dose would refer to the air surrounding each person who may be located in the open, in a house, or in a shelter that in it would refer to the dose shown by the dosimeter worn by each individual. Six per cent of this population

would require precautionary surveillance only, whereas 94 per cent would have to be hospitalized at the end of the latent phase. Sixty eight per cent of the population are expected to enter a serious clinical course followed predominantly by complete recovery, while 26 per cent are expected to exhibit a grave clinical course ending frequently in death.

From the standpoint of medical logistics, it is important to estimate incidence, onset, and duration of hospitalization as anticipated for an exposed population. When the data on dose dependency of the clinical course (discussed earlier) are combined with those on individual susceptibility, a graphic representation of such an estimate can be obtained (fig 7). To demonstrate the significance of figure 7, it shall be assumed that a large population has been exposed to 250 r. For this dose,

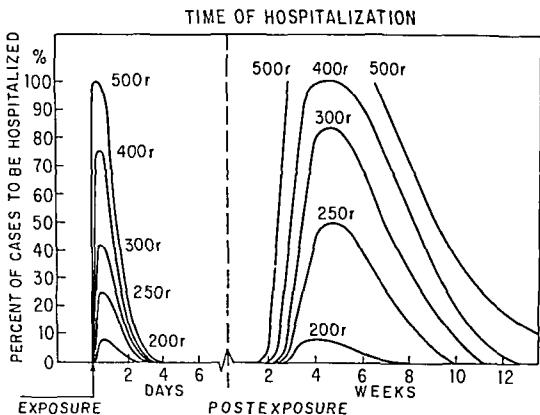


Figure 7 Estimate of incidence and duration of hospitalization for populations exposed to various amounts of penetrating ionizing radiation.

Figure 7 indicates that approximately 25 per cent of the people would be hospitalized during the first 2 days after exposure. Of course this might not be feasible under catastrophic conditions where the short period of hospitalization might not justify the efforts required to transfer a large number of casualties, however these persons would certainly require close medical attention. The large influx of patients to hospitals could be



expected to occur 2½ weeks postexposure. At the height of the disease—4 to 5 weeks postirradiation—about 50 per cent of the population would require hospital treatment. Thereafter the number of in house patients would be expected to decline rather rapidly with the last patient leaving the hospital at 10 weeks postexposure. In a similar fashion figure 7 may be used to estimate incidence, onset and duration of hospitalization for other dose levels. It must be stressed that the curves of figure 7 are based largely on extrapolation. Therefore future additional information will make correction possible but adjustments are expected to affect only minor details without changing the basic design of the figure.

#### INTERRELATIONS BETWEEN SIGNS, SYMPTOMS AND DOSE LEVEL

When a group of persons has been exposed to an unknown dose of penetrating ionizing radiation, diagnosis and prognosis must be based on developing signs and symptoms. The most important ones will be briefly discussed and evaluated.

##### Nausea and Vomiting

Absence of these prodromal effects is of eminent prognostic significance. It indicates with high probability that the air dose was less than 100 r, that the ensuing clinical course will be trivial in most cases, and that need for hospitalization will not arise. On the other hand, presence of these prodromal effects, even very early after exposure, does not imply poor prognosis as frequently stated. It strongly indicates, however, an air dose in excess of 100 r and therefore development of the acute radiation syndrome in most instances. Severity and outcome of the disease cannot be predicted from time of onset and degree of initial reactions since the two complexes are only loosely related. Nevertheless, persons showing prodromal symptoms should be closely watched for the appearance of further manifestations of the radiation insult.

##### Latent Phase

Onset of the disease after a 3 week latent period following remission of the initial reaction heralds the typical uncomplicated hematopoietic form of the acute radiation syndrome. In the majority of cases complete recovery may be achieved by proper management of the patients. Conversely, when a clear latent phase is not evident or when its duration is much shorter than 3 weeks, the early development of the illness foretells a grave clinical course probably complicated by gastrointestinal involvement. Prognosis is then poor.

## Fever

Stepwise ascending fever starting around the 20th day post exposure, even when associated with petechial and frank hemorrhage as well as with oropharyngeal infection, is typical for the pure hematopoietic form of the acute radiation syndrome and does not necessarily compromise its favorable outcome. In sharp contrast, high fever developing within 2 weeks post-exposure is a poor sign. With great probability it indicates gastrointestinal involvement since, most likely, it is a consequence of bacterial toxins or of bacterial invasion originating from the alimentary tract. The clinical course then must be expected to be grave and the outcome very dubious.

## Epilation

Loss of hair, when definitely caused by penetrating ionizing radiation, and not by alpha or beta emitters contained in fallout contamination of the skin, indicates an air dose in excess of 300 r. It is common radiotherapeutic experience that about 300 r are the smallest dose to cause temporary epilation. This sign is of prognostic importance for two reasons: (1) Generally it becomes noticeable as early as the end of the 2d postexposure week, that means it appears about 1 week before start of the actual disease, thus allowing sufficient time for precautionary measures. (2) After an exposure to more than 300 r a serious or grave clinical course must be expected; hence, epilation is the forerunner to the need for hospitalization. Therefore all persons observing excessive loss of hair after exposure to penetrating ionizing radiation should be kept under close medical surveillance.

## Diarrhea

Although transitory loose stool or diarrhea may occur occasionally as part of the prodromal reaction, they are not characteristic traits of the uncomplicated acute radiation syndrome. Opposing statements probably are derived from the fact that diarrhea was rather frequently observed among Hiroshima and Nagasaki casualties. Close scrutiny reveals, however, the widespread existence of this disturbance in the population of the two cities even before the attack. Nuclear accident and radiotherapeutic data prove beyond any doubt (see tables 1 and 2) that diarrhea does not belong to the symptomatology of the hematopoietic form of the acute radiation syndrome. Contrariwise, early and persistent diarrhea when definitely not caused by malnutrition or accidental infection is a rather serious sign. Very likely, it indicates exposure to more than 400 r and the existence of severe gastrointestinal damage. Prognosis is, at best, dubious.

## Leukopenia

As long as the total white blood cell count stays above 2 500 per  $\mu$ l, overt disease is not anticipated. Such a degree of radiation induced leukopenia is, in general, well tolerated and, with the exception of increased fatigability, does not seriously affect physical activity. When the count ranges between 2 500 and 1 000 per  $\mu$ l, the typical acute radiation syndrome will appear in most instances. Close attention is required with regard to the development of purpura, hemorrhage, and infection. Under proper treatment, prognosis is favorable. Counts below 1 000 per  $\mu$ l always will be associated with a serious or grave clinical course. The fact that in Hiroshima and Nagasaki leukopenias of such degree generally heralded fatal outcome is applicable only to practically untreated cases under catastrophic conditions. With suitable treatment in modern hospital facilities, even white blood cell values as low as 100 per  $\mu$ l may be handled successfully, as demonstrated by radiotherapy patients and nuclear accident victims. It should be reiterated that in the pure hematopoietic form of the acute radiation syndrome the minimal white blood cell count is encountered between weeks 4 and 6, and the cell drop frequently occurs rather abruptly. Therefore, in all persons suspected of having been exposed to appreciable amounts of penetrating ionizing radiation, hematologic examination must be performed regularly for 3 months, with particular emphasis on the critical time period extending from the 20th to the 40th day post exposure.

## Lymphopenia

The following dose ranges are probably indicated by the lymphocyte count during the first 48 hours postexposure: less than 50 r when there is no significant decrease; less than 100 r when the decrease is mild; and a dose in excess of 100 r when the lymphocytes fall below 50 per cent of normal values.

## TREATMENT OF THE ACUTE RADIATION SYNDROME

Since the therapeutic management of the acute radiation syndrome has been ably described by Cronkite, the ensuing brief survey essentially summarizes his views, with minor additions and modifications.

### Prodromal Complex

Most important is psychologic reassurance, emphasizing the transient nature of the disturbance as well as its relative insignificance with respect to the actual injury. In more serious cases, additional administration of sedatives is indicated—for example, chlorpromazine hydrochloride in oral doses of 25 mg every 6 hours. Only occasionally will vomiting be so profuse as to necessitate parenteral replacement of fluid.

### Cerebral Form

No experience is available excepting the fact that in animal experiments heavy sedation eliminates convulsive seizures

### Gastrointestinal Form

Since the alimentary tract will not tolerate anything other than small quantities of fluid, parenteral nutrition is mandatory. Water and electrolyte equilibrium must be maintained by large amounts of intravenous saline glucose, plasma, and balanced electrolytes. Around the end of the 1st postexposure week, when high fever and infection are expected to occur, antibiotic treatment should be started. Excellent nursing care and aseptic technic are paramount. Frank hemorrhage, anticipated during the 2d week, will require transfusions of fresh whole blood.

### Hematopoietic Form

Infection being the principal complication, careful examination of body temperature and oral cavity are necessary, particularly from the 3d postexposure week onward. The slightest evidence of infection is an indication for beginning antibiotic treatment. Cronkite does not recommend prophylactic administration of antibiotics because of two hazards—sensitization of the patient, and development of bacterial resistance. Purpura and frank hemorrhage require repeated transfusions of fresh whole blood or separated platelets and leukocytes. Frequency and amount of transfusions will be determined by the blood count. It may be worthwhile to try additional procedures in accordance with the usual management of agranulocytotic disorders. Figure 8 presents a graphic survey of the acute radiation syndrome in its hematopoietic form. The temporal relationship has been depicted for clinical course and therapeutic methods as applied in the *JF* group and the *MDA* series.

Some remarks concerning the effectiveness of the outlined therapy, especially that of the hematopoietic form, should be added. The frequently advanced concept of the treatment as purely symptomatic is too pessimistic. Hematopoietic depression and denudation of the gastrointestinal mucosa generally are transient, as are radiation induced epilation and azoospermia. Therefore, the therapeutic goal must be to help the patient overcome the relatively short period of time during which his own organism is not able to supply the critical cell elements. Hence, the transfusion procedures represent an actual substitution therapy. This fact can be demonstrated strikingly in animal experiments. In rats the minimal white blood cell count occurs around the 8th day postexposure. Parabiosis between an irradiated and a non-irradiated rat will carry the exposed animal through the bone marrow depression phase when adequate cross circulation exists.

between the 4th and 10th postexposure days longer parabiosis does not add to the beneficial effect. It is very likely that markedly improved treatment of the acute radiation syndrome

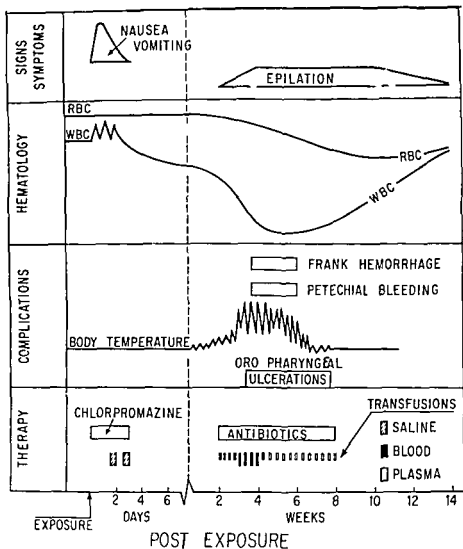


Fig 8 Shows the clinical course of the acute radiation syndrome. The graph illustrates the changes in hematology, complications, and therapy over time post-exposure.

will soon be possible as a result of current research efforts— injection of bone marrow or spleen material controlled cross transfusion with healthy donors and isolation of bone marrow stimulating substances.

Under the catastrophic conditions prevailing in Hiroshima and Nagasaki the mortality of the fully developed hematopoietic

form was 50 per cent. Among those patients who were treated at reasonably well equipped hospitals in Tokyo, the corresponding mortality was 30 per cent. With modern facilities, with sufficient types and amounts of antibiotics, and with the rapidly advancing techniques for the transfusion or exchange of fresh whole blood or any desired constituent of it, a much lower mortality rate can be achieved.

A discussion of some additional medical problems posed by nuclear disasters is contained in references 53 and 54.

### CONCLUSIONS

Since penetrating ionizing radiation has all the potentialities of becoming a major casualty causing agent, the peculiar clinical picture caused by this new type of injurious factor must be understood. Only knowledge can help to dispel the many uncertainties and misconceptions surrounding the radiation problem. Exposure of the whole body, or of a large part of it, to sufficient amounts of penetrating ionizing radiation induces in man the acute radiation syndrome. Clinical course and outcome of the disease are determined, in essence, by two factors—dose and individual susceptibility. At present, the factual evidence is not strong enough to establish with high accuracy the interplay between these factors in an exposed population. Since, therefore, most of the figures concerning incidence and severity of radiation induced injury must be based largely on extrapolations and estimations, their value is necessarily provisional and subject to revision when additional information becomes available. Nevertheless the following broad statements seem to be rather well supported by data originating from radiotherapy, nuclear accidents, and atomic bomb explosions. Air doses up to 100 r will be subthreshold for the acute radiation syndrome, and will thus be of no concern in emergency situations. In the dose range between 100 and 200 r, the acute radiation syndrome if it develops at all will proceed in such a mild form that it can be handled ambulatorily. The *hospitalization threshold*, a very important concept defined as that dose level beyond which hospitalization becomes necessary for an appreciable number of persons among a large exposed population, lies approximately at 200 r. Between 200 and 400 r—perhaps even 500 r—the acute radiation syndrome will be clinically significant and will occur in its hematopoietic form, displaying a very characteristic time course almost independent of dose. Knowledge of this time course should help in the advance preparation for medical personnel, supplies and housing facilities. With these steps taken and under proper therapeutic management the radiation induced disease will have a favorable outcome in the overwhelming majority of cases. All facts available disprove the fatalistic or pessimistic approach frequently encountered. In emergency situations

this dose range represents a great and rewarding challenge to the physician. Very little is known about doses above 500 r. Here, most likely a fulminating clinical course with gastrointestinal involvement will prevail and the outcome is at least dubious. Presently available facts are insufficient to either support or contradict the assumption that an acute exposure to 600 r is the highest one compatible with human survival.

The conclusion is that in a wide dose range man can overcome the acute radiation syndrome and return to a useful life. There exists no account of the many thousand survivors of Hiroshima and Nagasaki who resumed their previous occupation with full vigor while there are several reports relating each case of leukemia, cataract or neoplasm. Understandably as any other severe disease the acute radiation syndrome may be followed by late complications in a relatively small percentage of cases. Further observations must be made before an unbiased judgment is possible about incidence and importance of late consequences of irradiation.

### SUMMARY

From a comparative analysis of human data derived from nuclear accidents, Japanese bomb casualties, and radiotherapy patients emerges the clinical picture of the acute radiation syndrome with its three subdivisions—hematopoietic, gastrointestinal and cerebral forms. Dependency of the picture on dose level and individual susceptibility is discussed and the therapeutic management is outlined. Since penetrating ionizing radiation represents a potential casualty causing agent, problems facing the practical physician under catastrophic conditions are evaluated.

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# CARE OF THE PATIENT WITH BLOOD VESSEL INJURY

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**A**DVANCES in the field of vascular surgery have resulted in a significant reduction in the amputation of limbs following trauma. The military medical services have contributed substantially to these advances as evidenced in the recent Korean conflict.<sup>1-4</sup> Inasmuch as vascular surgery is a relatively new field, this subject is presented further to familiarize the military medical officer with the care of the patient with major blood vessel injuries.

For patients with injury to the major vessels of the abdominal and thoracic cavities live to reach a hospital; therefore, most surgery of acute vascular injuries involves the peripheral vessels, but injuries to these vessels require prompt surgical attention. Because vascular surgery is urgent surgery, it is most important that every surgeon confronted with the care of patients with acute vascular injuries constantly keep in mind the basic principles of management of the wounded. Patients with major blood vessel damage are usually in poor condition. It is essential therefore that they be properly resuscitated and evaluated for priority of care of all injuries and for ability to tolerate any additional time required for vascular surgery. Failure to observe these basic principles may result in a loss of life in an attempt to save a limb.

## PREOPERATIVE CARE

Vascular injuries may be presented as open wounds, varying from minor lacerations to avulsions, or as occlusions resulting from spasm, emboli, displaced bone fragments, or other complications or trauma. A differential diagnosis may be difficult but when in doubt the patient should be treated as having a vascular injury. A cold, pulseless limb may result from exposure, shock, spasm, compression, or from arterial injury. External hemorrhage may or may not be present. An accurate diagnosis often cannot be made until wound debridement, although a wound in the vicinity of a large vessel should arouse suspicion of vascular injury.

Comparison of pulses color and skin temperature in the two extremities should be helpful in making a diagnosis. Regardless of the type of injury the objective of treatment is restoration of arterial blood flow at the earliest possible moment.

Definitive surgery may not be feasible in the area of initial care. However, the diagnosis should be made, preliminary management begun, and plans made for emergency evacuation. When the situation dictates transfer of the patient, evacuation should be facilitated as soon as the condition permits. During resuscitation it is preferable to replace tourniquets with pressure dressings for the control of hemorrhage. In rare instances a tourniquet may be required but most pressure dressings applied with an elastic bandage can be applied as tightly as a tourniquet if necessary. In wounds exposing the damaged vessel clamps may be applied to the open ends of the vessel for control.

### OPERATIVE CARE

After arrival of the patient at an installation where vascular surgery is available under anesthesia the operative site is prepared by shaving and scrubbing and the wound is irrigated with sterile saline solution. The presence of a pneumatic tourniquet for use at surgery is desirable whenever applicable but should be left uninflated except when actually required. In large wounds the ends of the vessels may be visible and controlled directly otherwise an anatomic approach to the injured vessel is used regardless of the wound location. The artery is approached first proximal then distal to the site of damage control tapes are placed about the vessel and dissection is carried toward the point of arterial injury. After the artery is controlled attention then is given to debridement of the wound which must be debrided thoroughly and irrigated as in any traumatic wound.

The vessel must be examined to determine if there is more than one site of injury. Vessel wounds created by tiny missiles may appear benign but on closer examination the small area of trauma may be found to extend for some distance. Small wounds often are plugged by a clot which extends into the lumen masking the injury and serving as a focus for thrombosis or embolism. Frequently missiles also perforate the opposite wall. Such wounds if not properly treated may result in secondary hemorrhage occlusion of the artery or the development of a false aneurysm.

The treatment of an arterial injury resolves itself into three categories (1) repair (2) ligation, and (3) conservative or non operative management with delayed definitive care.

**Repair.** An artery partially lacerated by a sharp instrument with negligible contusion may be sutured simply with minimal debridement. The more severely lacerated or severed vessel must be debrided in accordance with the surgeon's best judgment. Repair

is preferably by anastomosis when possible (fig 1), and the majority of repairs can be accomplished in this manner. In general up to 2 cm of vessel can be sacrificed and still permit anastomosis. Judgment as to the amount of tension that an anastomosis will stand comes only with practice. When repair by anastomosis is

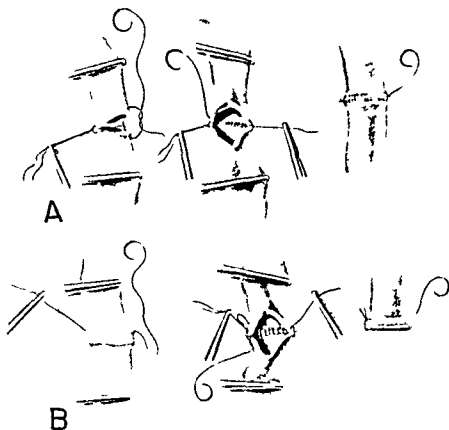


Figure 1 A demonstrates the steps of anastomosing a vessel using a continuous over-and-over suture B demonstrates the use of a continuous transverse mattress suture for comparison with the simple suture method shown in A

not possible without undue tension, a graft must be inserted. A homologous artery graft or an autogenous vein graft (fig 2) may be used. Veins accompanying the artery are usually too large for use and, furthermore, should not be sacrificed but should be preserved whenever possible.

After arterial repair it is imperative that the vessels be covered for nourishment and protection from infection. Viable muscle and subcutaneous tissue are satisfactory, while fascia, because of its poor vascularity, is not. Furthermore, the site of vascular suture must not be wrapped in some impervious foreign material which prevents revascularization. Coverage of the vessels does not imply closure of the wound.

Care also must be taken to protect suture lines at joint sites. Such extremities usually are fixed in 15 to 20 degrees flexion following

repair to reduce tension at the suture line. During the healing period the extremity must be taped or splinted to prevent violent extension with separation of the suture line. The same care must be exercised with patients having vascular repairs in the presence of fractures. Excessive traction may result in rupture of the suture

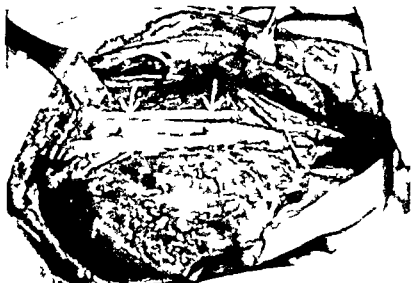


Figure 2. A. A photograph of a vascular graft anastomosis. The graft is sutured to the host vessel. The surrounding tissue is covered with a bandage.

line or displacement of the bone fragments may lacerate or compress the repaired vessel. A well padded basket or splint should be used to hold the fracture in position. Undue constriction and pressure from casts must be avoided for 10 to 15 days until healing of the vessel has occurred.

**Ligation.** There are indications for ligation of major vessels. This procedure may become necessary when the condition of the patient will not permit the additional time required for surgical repair. In large avulsed wounds where coverage of vascular grafts is impossible, ligation also may be utilized. When evacuation to a center equipped for vascular repair is impossible, then ligation of the vessels should be performed rather than leave a tourniquet in place and delay debridement indefinitely. Even if facilities are present, ligation may be necessary because of the large volume of cases and inability to spare time for limb-saving at the expense of livesaving. With ligation procedures one may expect an over all incidence of gangrene in approximately 50 per cent of the limbs where major vessels are ligated. The incidence of gangrene varies from 70 to 100 per cent for the more critical arteries such as the popliteal to from 25 to 30 per cent from

ligation of the brachial artery below the profunda Elective ligation of the concomitant or companion vein at the time of ligation of the artery is contraindicated Ligation of minor arteries such as the profunda in the arm and thigh, or one of the small arteries in the forearm or leg, does not endanger survival of the extremity Even though ligation of a vessel may not result in gangrene, it frequently results in arterial insufficiency

**Conservative Treatment** An artery may be partially severed with little or no evidence of external hemorrhage but develop a pulsating hematoma When both artery and vein are injured, an arteriovenous fistula may be formed, with flow of blood directly from the artery to the vein Patients with such injuries, with controlled hemorrhage and viable extremities evidenced by distal palpable pulses, should be given a lower priority for surgery Conservative care is particularly applicable to wounds of the carotid and subclavian arteries with controlled pulsating hematomas

Patients treated conservatively should have minimal wound debridement with care taken not to dislodge the clot and to avoid wound infection Careful observation is necessary for expansion of the hematoma with compression of vital structures (fig 3) hemorrhage, or infection

### COMPLICATIONS

While there is no great mystery surrounding vascular surgery, there are a number of seemingly minor but important details which contribute to successful blood vessel repair with minimum complications Lack of facilities is certainly an indication for prompt evacuation as soon as the patient is in condition to travel Although a competent surgeon may be present, necessary instruments may be lacking The reverse situation—with proper instruments available to the untrained surgeon—may be more disastrous It is extremely beneficial to have developed technic in an experimental laboratory, or to have assisted with vascular surgery prior to operating on one's first patient Attempts of the surgeon inexperienced in vascular surgery to repair blood vessel injuries have resulted in tragedy Loss of the patient's life is likely to be the result of the eager surgeon who fails to evaluate properly and resuscitate the patient before rushing him to the operating room in an attempt to save a limb The same disaster may occur from unwisely prolonging surgical intervention by the additional time required to perform blood vessel repair following other major abdominal and thoracic surgical procedures Lives also have been lost from opening a pulsating hematoma without adequate proximal and distal control of the vessels entering the hematoma Limbs have been lost by the inexperienced surgeon who has opened pulsating hematomas and found, to his despair, that he could not repair the arterial damage Limb loss also has resulted from

attempted repairs in which collateral branches were sacrificed to permit anastomosis of the vessel only to have the anastomosis fail from constriction, spasm or thrombosis



Fig 3 A p l s a t g hematoma d m t t d th p p l t a l p W b l  
the h m a t m a l f c o t a d a d t h e x t m t y s b l w l l g o f t h  
l g r d e t B c a s o f t h t g h t p p l t l p e x p a o o f t h e h m  
a t o m t h a a c a u l t n l y d a m g h e m i t o t h l g

The most important cause of limb loss is time lag from injury to arterial repair. Best results are obtained in those patients having repair within 10 hours of injury. This does not mean that there should be a time limit beyond which an arterial repair should not be done. There are many variables that make it impossible to set a time limit for repair. Because it is not always possible to judge clinically the irreversibility of ischemic muscle, it is good practice to repair major blood vessel injuries even when in doubt of irreversibility of damage. With restoration of the blood supply to muscles of questionable viability the patient must be observed for evidence of acute renal failure. Evidence of renal involvement with decreased urinary output and increased serum potassium and nonprotein nitrogen levels may be an indication for early amputation of the nonviable limb or excision of necrotic tissue.

Frequently the ischemic limb exhibits a contracture resembling Volkmann's contracture. This may be reversible if the blood supply

is restored in time. Upon restoration of blood flow to such limbs, the muscles tend to develop edema as a result of the ischemic changes, and, if fasciotomy is not performed, the continued volume increase of the muscle within the closed fascial compartment results in the compression of vessels, nerve damage, and necrosis of tissues. Failure to recognize this process has resulted in permanent nerve damage and loss of compartments of muscles and extremities following an otherwise satisfactory vascular repair (fig 4)



*Figure 4. Here the late results of Volkmann's contracture and ischemic swelling are noted. Admitted with axillary artery and upper arm injuries the limb muscles were ischemic and contracted. Following repair of the axillary artery swelling of the forearm occurred and fasciotomy was performed too late to preserve the flexor muscles.*

When segmental spasm occurs following arterial injury it often can be treated successfully by the use of 2.5 per cent papaverine hydrochloride<sup>6</sup> or 1 per cent procaine hydrochloride applied locally to the spastic segment. Generalized spasm of the arterial tree may be improved by sympathetic block with 1 per cent procaine hydrochloride or spinal or caudal anesthetic block may be given as a single or as an intermittent or continuous application, as indicated.

Anticoagulants are not indicated in these cases and may lead to serious hemorrhage particularly in the patient with multiple injuries. The complications of hemorrhage from the vascular repair should not be a problem if the vessel has been properly debrided, properly sutured without undue tension, and properly covered and



protected from abnormal stress at joint and fracture sites. Infection that also will cause hemorrhage or thrombosis should not be a complicating factor if the wound has been properly debrided and cleansed. In order to ensure further against infection antibiotics may be given for approximately five days but antibiotics should not be used as a substitute for good surgery. There is no substitute for careful resuscitation and evaluation of the injured patient before surgery.

### SUMMARY

The essentials of care of the patient with blood vessel injury are presented in order better to acquaint military surgeons with accepted concepts. As always in trauma cases assessment of the total injury, resuscitation and adherence to priorities in treatment are of extreme importance often making the difference between life and death and saving or losing a limb. Treatment of arterial injury falls into three categories: (1) repair, (2) ligation and (3) nonoperative management with delayed definitive care. Specific indications for each exist. Judgment as to what to do and when to do it, coupled with technical skill developed before the emergency, arises, will save limbs and lives. Improper hemostasis, lack of technical training and poor judgment result in loss of life and limb.

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# FIVE TO NINE YEAR FOLLOW UP OF PULMONARY RESECTIONS FOR TUBERCULOSIS

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**T**HE PURPOSE of this paper is to report a five to nine year study of 59 consecutive patients with pulmonary tuberculosis who had their major foci of disease removed by segmental and subsegmental resection during the period January 1948 to September 1952. Local enucleations of superficial lesions are not included.

In 1953 Chamberlain and associates<sup>1</sup> reported on 300 similar cases followed for from one to five years. They described the indications for surgery and the operative and postoperative management to which we have adhered at this hospital. Both the technique and the management used in our cases were those developed by Chamberlain.<sup>2,3</sup>

In the present era of antituberculosis drugs, segmental resection has become well established both here and abroad as a reasonably safe method by which the tuberculous patient may be separated from his caseous, fibrocaseous, and cavitory, residual, necrotic foci.<sup>4-7</sup> Most of the patients reported on in this paper, however, had their resections prior to the current "drug era." Many of them were inadequately covered by drugs at the time of operation; many were re-treatment cases, and others had had previous surgical maneuvers to control their disease.

Since 1952 there has been more uniformity of treatment. The majority of the patients now come to the surgeon having had at least six months of drug therapy as a "first course," without prior surgical intervention, and with negative sputums. Because of these advances, as well as better selection of patients for segmental resections, the more recent results have shown marked improvement. There have been no surgical deaths and only two

serious complications in our last 146 patients operated on for tuberculosis by this technic

The average age of the patients in the present study was 33 years the youngest being 19 and the oldest 56 Four of the 59 patients are dead and 55 are living Of the living 53 are well and capable of working 1 had a recent reactivation that at present is under control by drugs and 1 is untraced although known to be alive There is thus a 98.3 per cent follow up

The mortality in this series has been 6.8 per cent over a five to nine-year period In only one of the four cases where death has occurred was the cause of death directly related to tuberculosis The immediate operative mortality was 1.7 per cent the total 3.4 per cent One patient had a postoperative hemorrhage with acute tubular necrosis and death in uremia Another patient after multiple operations required pneumonectomy to control a broncho pulmonary fistula with empyema and died from an anesthetic accident 20 minutes after the operation The remaining two patients each lived for four years postoperatively and died of coronary occlusion

The location of the tuberculous foci is shown in table 1 There was a predominance of left sided disease in this series This was particularly evident in regard to apicoposterior resections of which there were 22 on the left but only 13 on the right The small size of the series makes this perhaps more interesting than significant Examination of the pathologic reports of the resected specimens revealed that there were 15 patients with cavities as the predominant lesion 40 with fibrocaseous involvement and 4 with tuberculous granulomata

TABLE 1 Location of tuberculous foci in 59 patients

	Right	Left	Total
Segment	35	52	87
Subsegment	7	10	17
Total	42	62	104

In 13 patients there were early complications These are listed in table 2 together with the operation performed the result of a sputum examination at the time of operation the treatment of the complication and the present status It has been stated that the degree of activity of the disease at the time of operation does not influence the complication rate In this series it may be significant that the sputum was positive in each of the four

TABLE 2 Early complications seen in 13 of 59 patients

Case	Segmental resection performed	Sputum at operation	Complication	Treatment	Present status
1	AP LUL	Positive	Space	Thoracoplasty	Well
2	ANT & AP RUL	Positive	Space	Thoracoplasty	Dead coronary occlusion
3	AP RUL	Positive	BP fistula & empyema	Thoracoplasty & pneumonectomy	Dead anesthetic accident
4	AP LUL	Positive	Space	Thoracoplasty	Well
5	AP LUL	Positive	Space	Phrenic crush	Well
6	AP RUL	Negative	Space	Thoracoplasty & decortication	Controlled under 2nd Rx course
7	RML	Negative	Space	Thoracoplasty	Well
8	AP RUL	Negative	Hemorrhage	Thoracotomy	Dead acute labular necrosis
9	ANT RUL	Negative	Space & positive culture	Refused operation	Well after homolat spread
10	SS LLL	Positive	BP fistula	Thoracoplasty & myoplasty	Untraced (living)
11	AP LUL	Negative	Space	Pneumoperitoneum & phrenic crush Refused thoracoplasty	Recently stable
12	AP LUL SS LLL	Positive	BP fistula	Thoracoplasty	Well
13	AP RUL	Positive	BP fistula	Closure of fistula & thoracoplasty	Well
AP apicop sterior LUL left upper lobe (et cet ra)				BP bronchopleural SS superior egm nt	

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following operation in March 1951. Contralateral reactivation was stabilized by a second course of drugs, and he is now well. A 20-year old man had a persistent space after resection of the anterior segment, right upper lung in October 1951. He developed a positive culture three months after the operation, and an ipsilateral upper lobe cavity within a year. Following a second course of drugs in 1953, he is now working, with inactive disease.

### DISCUSSION

The chief value of this paper derives from the long follow up of consecutive patients who were operated upon in the 1948 to 1952 era. Although the results obtained in this series compare favorably with other similar series of segmental resections, future reports should show improvement in the rates of complications and mortality because of (1) preoperative drug schedules which are more uniform and effective, (2) proper selection of patients at the operating table for the segmental type of operation, (3) a larger percentage of primary treatment cases and cases without such extensive disease as was seen formerly, and (4) greater familiarity of the surgeon with the strategic maneuvers attendant upon postoperative care.

Certain technical refinements in current use, not necessarily original with us, include the following: (1) early division of the bronchi, (2) use of extrapleural dissection in the cupola of the chest to facilitate the handling of dense, vascular adhesions, (3) occasional construction of an apical pleural tent in the hope of preventing intrapleural space problems, and (4) suturing of the segment or segments remaining, to the adjacent lobes in such a manner as to prevent torsion, and where possible, to cover the raw surfaces.

Some authors have mentioned placing streptomycin sulfate and penicillin in the pleural cavity, the use of one lower tube, and gentle postoperative suction.<sup>9</sup> We have preferred not to use intrapleural drugs, have used two tubes, and as much suction as is necessary to stay ahead of leaks. Gale and co-workers<sup>8</sup> warned against the use of strong suction in the presence of atelectasis and air leaks. Pacheco and associates<sup>10</sup> believed that the incidence of fistulas is related to the "existence of a residual pleural cavity."

Bickford and associates<sup>4</sup> preferred immediate thoracoplasty if more lung volume than two segments is removed. We have not followed any rule, preferring to assess each case at the operating table in the light of estimated lung thorax compliance. Bell<sup>11</sup> reminded us that thoracoplasty should be done early enough in the control of postoperative complications to preclude the development of rigid walls. He also pointed out that many postoperative

spaces are negative or neutral in pressure and may respond to conservative measures. Wareham and co workers listed certain criteria for the conservative management of postoperative spaces: (1) absence of symptoms (2) progressive shrinkage of the space (using tomograms) (3) negative sputa and (4) effective antibiotics.

Each of the foregoing factors merits careful consideration with individual assessment of each patient. Assiduous attention to operative and postoperative detail is of vital importance and as Thomas mentions this will keep errors related to the human factor at a minimum.

### SUMMARY AND CONCLUSIONS

Fifty nine consecutive cases operated upon by segmental resection for tuberculosis five to nine years prior to September 1957 are presented with a 98.3 per cent follow up. Of 55 who are living 53 are well enough to work, 1 is living with recently arrested disease, and 1 is untraced although known to be alive. Four are dead, two of unrelated causes, one an operative mortality, the other because of an anesthetic accident following successive operations for persistent tuberculosis. The operative mortality was 1.7 per cent and the incidence of serious bronchopleural fistulas 6.8 per cent. Reactivations of the disease were five in number, three homolateral and two contralateral. All were controlled.

Certain aspects of the surgical treatment of pulmonary tuberculosis are discussed with references to recent similar series of segmental resections. It is concluded that this procedure as demonstrated by long term follow up is a safe and effective method of treating tuberculosis. Even *without* our present day use of adequate drug therapy segmental resection proved to be an effective method of treatment. With modern drug coverage it has been demonstrated to be safer and should prove to be still more effective.

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## RECREATIONAL THERAPY IN PSYCHIATRY

Dr Hack Tuke who is to my mind one of the most neglected of the psychiatric classicists and who with Pinel was perhaps the most significant psychiatrist of the early 19th Century had noted at his private sanitarium The York Retreat an interesting and for that period a remarkable observation namely that psychiatric illness did not seem to so largely affect members of the artisan class Only 50 years earlier Europe had been astounded to learn that King Louis XVI of France found it relaxing to employ as a hobby the trade of a locksmith which he had learned from a servant as a boy and we read that he passed the long months in prison prior to his execution by repairing locks Tuke who discovered this took this lesson to heart and despite the resistance of both his patients and the medical profession organized a series of little craft shops in The York Retreat and was the first to describe the beneficial results which accrued to patients by work of this nature He gradually came to learn as we now know so well that all work and activity in the hospital may have a therapeutic as well as an educational value for the persons who undertake it "

—C W WAHL M D

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# REQUIREMENT FOR REDUCTION IN ANTIBIOTIC DOSES DURING OLIGURIA

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IT IS well established that many antibiotics are excreted principally in the urine and that the size and frequency of antibiotic doses should be reduced during renal insufficiency.<sup>1</sup> In spite of this information many physicians continue to prescribe antibiotics according to rules of thumb without regard for diminished excretion during oliguria. In addition some texts on the management of renal insufficiency either neglect to mention this important point or advise antibiotics in full doses for pyelonephritis with oliguria which cannot always be distinguished from nonbacterial renal disease. As a result a high proportion of the patients with oliguria (less than 500 ml of dilute urine per 24 hours) arriving at this hospital have exceedingly high blood concentrations of antibiotics. The toxicities of antibiotics are familiar to all and will not be reviewed here. The purpose of this report is to document the adequacy of small infrequent doses and to re-emphasize the need for a flexible regimen.

## METHODS

The streptomycin and tetracycline assays were performed by the streptomycin method of Romansky and Bedsole<sup>2</sup> and the penicillin and erythromycin assays by the serial dilution tube technic of Rammelkamp<sup>3</sup> both modified to give a maximum reading of 100  $\mu$ g or units per ml.

## CLINICAL MATERIAL AND RESULTS

Random analyses for antibiotic concentrations in the blood of 12 oliguric patients revealed values in excess of 100  $\mu$ g of streptomycin per ml in 4 patients, 100 units of penicillin per ml in 7 patients, 150  $\mu$ g of erythromycin per ml in 3 patients, 67  $\mu$ g of tetracycline per ml in 3 patients, and lesser but still excessive concentrations of these and other antibiotics in several additional patients. The administration of antibiotics where recorded had

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been in the range usually employed in patients with normal renal function. In general, the blood concentration of streptomycin exceeded the therapeutic range by a greater percentage than that of other antibiotics also administered in standard doses. Because of this observation and the more serious toxicity of streptomycin, it was selected for further examination in oliguric patients.

The blood concentration of streptomycin was assayed in 10 oliguric patients who had been receiving streptomycin prior to admission. Although the previous dosage schedule was not surely known in all instances, several patients had no record of having received any antibiotic during the preceding day or two, when they were in transit from an overseas hospital. In 8 of the 10 patients, blood was drawn on admission for the initial determination, after which 0.5 gram streptomycin was administered to each patient. The blood concentration of streptomycin was first determined on the remaining two patients on the day after admission. During the next few days no antibiotic was given to any of the 10 patients and the blood concentrations were assayed repeatedly.

As shown in figure 1, seven of the eight patients examined on admission already had blood levels in or above the therapeutic

$\mu\text{g/ml}$

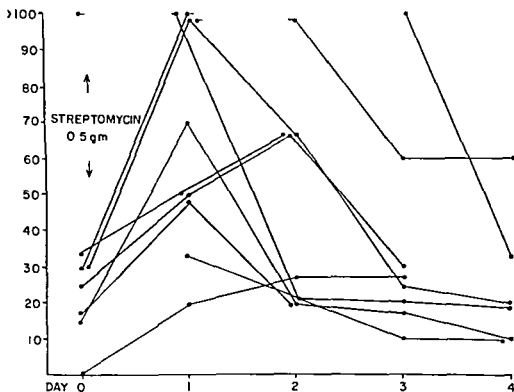


Figure 1. Streptomycin concentration in the blood of 10 oliguric patients. After blood for assay was drawn from 8 of the patients on day zero, each of the 8 patients received 0.5 gm of streptomycin. No antibiotic was given to any of the 10 during the next 4 days.

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## SALICYLATES AS A CAUSE OF GASTRIC HEMORRHAGE

Salicylates may cause bleeding from the gastrointestinal tract by several mechanisms operating either singly or in combination. These are by the production of hypoprothrombinaemia by local tissue irritation by gastric allergy by an increase in gastric acidity and by an effect on the gastric mucous cells or on mucin itself. The administration of salicylates appears to increase the frequency of bleeding in patients with proven peptic ulcers but apart from this it is clear that a small group of subjects are much more susceptible than others. An observed seasonal incidence of peptic ulcer activation may be partially explained by the more frequent use of aspirin in the ulcer months which coincide with the peak period for upper respiratory tract infections and minor illnesses such as the familiar flu for which the usual treatment is aspirin with rest.

All patients who suffer from upper gastrointestinal hemorrhage should be questioned concerning the use of salicylates or proprietary drugs containing salicylates. This needs to be done with care as aspirin is an almost universal form of self medication and many people would fail to think of it as a drug. A little trouble taken in clearing up this point may spare a patient future episodes of bleeding and les operation (for subtotal gastrectomy has been carried out for bleeding probably due to aspirin ingestion) and perhaps even his life.

—EDITORIAL

M d l J m l J Aust l  
pp 832 833 D 1 1956

# REPAIR OF CRANIAL DEFECTS WITH ANTERIOR ILIAC BONE GRAFTS

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**A** PROBLEM confronting surgeons at an overseas center is the return of all salvageable patients to active duty. Patients with large cranial defects following depressed skull fractures, especially those involving the frontal sinuses, previously were evacuated to the United States from our hospital. The danger of secondary infection in such wounds was considered so great that early cranioplasties employing the inert metals or plastic resins were not performed.

The early repair of very large cranial defects with autogenous bone was considered more feasible because of the reduced incidence of infection with such grafts. The difficulty in obtaining the graft, the size and shape of a readily obtainable graft, and the added risk and discomfort to the patient were evaluated for the usual donor sites—tibia, rib, ilium, et cetera. One of us (T H C)<sup>1</sup> previously had taken a large number of grafts from the anterior crest of the ilium for other purposes. The procedure was simple and did not cause serious discomfort or ensuing debility. Furthermore, the shape of a split-thickness anterior iliac graft corresponded to the contour of the skull, and large grafts were readily available.

The following report concerns an initial study of 12 cranioplasties accomplished with autogenous split thickness grafts from the anterior crest of the ilium.

## METHOD

The use of iliac bone as an autogenous source for bone grafting procedures has been increasingly popular. This popularity is justified because of the ready availability of a generous amount of bone, the general lack of complications following the removal of graft from the donor site, and the rapidity with which the cancellous bone from the ilium usually unites with the recipient bed.

In this series it has been our practice to take a split-thickness graft resecting and using only the outer cortex of the anterior portion of the ilium. This has provided a generous source of bone in one solid sheet which with its natural smooth concave cortical surface has been found to fit accurately against the dura mater leaving the cancellous surface in juxtaposition to the rich blood supply of the scalp. Furthermore by leaving one cortex of the ilium intact the contour of the pelvic girdle is undisturbed and no appreciable structural defect is produced nor is muscular strength of the leg and thigh impaired.

Because cranioplasty is an elective procedure the technic of securing the graft is preceded by 24 hour preparation during which the pubic area and donor site are shaved and scrubbed with pIisoHex (brand of hexachlorophene) and then covered with sterile dressings. In the operating room the skin is scrubbed again with pIisoHex and draped in the usual sterile manner.

The incision is started at the anterosuperior crest of the ilium and directed backward along the crest for the required size of graft needed. The incision is carried through the periosteum longitudinally at the mid portion of the crest at about the junction of the attachments of the abdominal and gluteal muscles. The periosteum with the origin of the gluteal muscles is then stripped from the lateral cortex of the ilium using a periosteal elevator or a bone chisel where the strong fibrous attachments require a sharp dissection. Usually it is not necessary to detach the attachment of the tensor fasciae latae the sartorius or the inguinal ligament from the anterior superior iliac spine as this projection of the bone seldom is required in the pattern of the defect. Their strength can thus be unimpaired though it certainly is permissible to use this portion of the bone if needed. In such case one should be careful to avoid the lateral femoral cutaneous nerve. Cutting this will cause bothersome anesthesia of the thigh and on occasion painful neuromas.

The bone is secured best by using a cloth pattern taken from the cranial defect prior to surgery and sterilized so that it can be placed against the outer cortex of the ilium as a guide. The pattern can be outlined by incising the cortex with a sharp osteotome and the graft removed by splitting the ilium sagittally from the crest with a broad blade osteotome. In young patients who have not yet completed their growth the epiphysis is left undisturbed and the graft resected from an area at least 1 cm proximal to the epiphyseal line. The cut edges of the ilium are impacted and the gluteal muscles are reattached to the periosteum at the remaining crest of the ilium. These muscles act as a tampon and to a large degree prohibit bleeding from the raw bone. It is advisable however to insert a rubber drain down to the bone from the posterior extremity of the wound to prevent

the formation of a hematoma and possible disruption of the wound. The drain should be removed in 24 to 48 hours. The subcutaneous tissues and skin are approximated in the usual manner.

In the meantime, the neurosurgeon will have exposed the cranial defect, and the bone graft now can be shaped and fitted to fill the skull defect. It has been our practice to bevel the edges of the cranial defect with a sharp chisel, so as to provide a new raw bone surface against which to place the conversely beveled bone graft. Usually, the bone graft has fitted so snugly into the cranial defect that retaining sutures were not needed. Occasionally it has been necessary to use wire sutures to hold the graft accurately in place. These are secured by drill holes made through both cranium and graft, taking care to bury the cut ends of the wire in the bone to prevent irritating the scalp.

### RESULTS

In this series of cases, 12 patients with moderate to large sized cranial defects were selected for repair of their bony defect with split-thickness or full thickness iliac bone grafts. All but one of the cranial defects had resulted directly or indirectly from severe trauma to the head. There were a number of depressed skull fractures that were grossly contaminated through a compounding injury. Three patients were operated on shortly after suffering a compound depressed skull fracture involving the frontal sinuses. In two of these, the cranioplasty was undertaken in the face of sinus infection without adverse results.

In every case a satisfactory structural and cosmetic result was obtained with the iliac bone graft. One patient, who was operated on before the residual of a severe brain stem injury had resolved, represents the one case of postoperative morbidity in our series. After operation, he had a pseudobulbar palsy that lasted for nearly four weeks before complete recovery ensued.

Pain from the donor site was usually more marked than pain from the site of cranioplasty. In one case, persistent iliac pain was coincident with a persistent fluid hematoma at the graft site. This disappeared entirely after 10 days, however, and in all the other cases iliac pain and pain from the cranioplasty site had disappeared by the third postoperative day. One patient who had been immobilized for a long period because of an associated compound tibia fracture, developed thrombophlebitis after the postoperative period had elapsed. This was treated successfully with anticoagulants and mobilization.

### CASE REPORTS

**Case 1** A 6-year old boy was hit on the side of his head with a pump handle causing a large compound depressed skull fracture. This was

elevated on the day of injury 13 May 1955 with removal of the bulk of the contaminated fragments. Neurologic recovery was complete and the only remaining stigma was a large parietotemporal defect. On 5 August a right iliac bone graft was applied to the defect. The bony edges of the craniectomy site were prepared with an electric bur instead of the chisel and osteotome used in the other cases. The cosmetic result was satisfactory and roentgenograms taken a year later indicated beginning calcification of the graft site.

C 2 A 26-year old staff sergeant received a head injury in a motor cycle accident on 2 July 1955. He had a compound depressed skull fracture on the right. On 13 July he was transferred to this hospital where the depressed skull fracture was elevated and a rather large extradural hematoma was evacuated. The patient who was somnolent, disoriented and lethargic with a dilated right pupil when he came in recovered almost completely except for the cranial defect. Three months later a split thickness anterior iliac bone graft was applied to the craniectomy site. The immediate postoperative cosmetic result was satisfactory. Roentgenograms of the patient's skull taken postoperatively revealed a well fitting calvarial plate which did not necessitate retaining suture. Because of legal complication this patient had to be shipped back to the United States before an adequate follow up examination could be made.

C 3 A 20-year old man was injured twice in a jujitsu wrestling match. He developed a right hemiparesis two weeks after his injury and a craniectomy of the right parietal region was performed to evacuate a substantial subacute subdural hematoma. On 9 September 1955 a split thickness iliac bone graft was used to repair the craniectomy defect. A one-year follow up on this patient revealed a good cosmetic result. The patient had no complaints referable to his cranioplasty site and had participated in swimming meets without adverse effects. Skull roentgenograms done at this hospital revealed the obliterated defect in the right frontal parietal region with the bone graft in place.

C 4 A 45-year old woman fell down a flight of stairs and suffered a compound depressed skull fracture in the left frontotemporal region. During elevation of this fracture a large extradural hematoma was visualized and evacuated. The patient who preoperatively was lethargic and unable to carry out rational conversation recovered to a completely normal neurologic state. On 6 December 1955 the usual split thickness iliac bone graft was used to repair the craniectomy site. This patient was seen 10 months later before she returned to the United States. The graft was solid and painless on palpation. The cosmetic result was satisfactory enough so that it permitted her to act as hostess for large official military gatherings without apprehension as to her appearance.

C 5 A 21-year old man was injured in an automobile accident on 17 December 1955 and sustained a deeply depressed compound frontal

skull fracture. He had a large craniectomy in the frontal region with elevation of his depressed fracture and obliteration of the greater part of his frontal sinuses. On 6 April 1956 a right iliac split thickness graft was used to repair the frontal defect. The patient had a further debridement of sinuses at the time of the cranioplasty. One sinus was packed with fat and the other with bone chips for comparative test. The cosmetic result was considered to be excellent. In the postoperative period the patient had severe attacks of maxillary sinusitis but his frontal sinuses remained uninfected. The patient was asymptomatic on 26 December.

**Case 6.** A 3 year-old girl fell out of a second story window and suffered a compound depressed skull fracture in the right parietal region. The fracture was elevated and the inferior bony segments which protruded into the brain were removed. The patient had a plastic repair of her dura mater after debridement of the cerebral wound. Although she was unconscious when she came in with active bleeding from both ears she recovered completely after this procedure and had no residual except for a craniectomy defect. On 27 June 1956, a split thickness iliac bone graft was taken and a cranioplasty was accomplished. The result has been good. The patient remains asymptomatic and a six month recheck examination disclosed a solid graft without pain on palpation.

**Case 7.** A 23 year-old man had a granuloma of the skull with severe radiating headaches. A primary resection of this bony tumor and iliac graft were planned for 25 January 1956. A split thickness iliac bone graft was taken from the left anterior crest of the ilium but the patient suffered a cardiac arrest and had to be resuscitated by means of a cardiac pacemaker. On 3 February the cranial lesion was resected under local anesthesia and was found to involve the dura mater. The histologic diagnosis of granuloma however was made on rapid section and total resection of the tumor was accomplished. The iliac bone previously taken and kept in the deep freeze bone bank was used for a cranioplasty. This patient with a low pain threshold has had no complaints about either the donor site or cranioplasty since the operation.

**Case 8.** A 20-year-old man was involved in an automobile accident in late May 1956 suffering severe head injuries. He was deeply unconscious and began to have decerebrate seizures. The patient had massive brain swelling and a bilateral temporo-parietal craniectomy was performed on both sides with a large free dural graft taken from the temporalis fascia to give a watertight dural closure. The patient gradually recovered consciousness over a period of several months and his only residuals were a paralysis of upward gaze and signs of a frontal lobe disturbance.

On 24 July 1956 a full thickness iliac graft was taken and bilateral cranioplasty was carried out under general anesthesia. After this procedure the patient suffered a pseudobulbar palsy with difficulty in swallowing in jaw movements and in tongue and facial movements.



along with some increase in the emotional lability that was present to some extent before the operation. His symptoms lasted for almost a month before gradually improving to the extent that he could speak English and German and could use with facility all the muscles innervated by the lower cranial nerves. This man became use of his severe central nervous system damage was returned to the United States for prolonged hospitalization. At this time both graft sites were well healed and solid to palpation.

C 9 This patient was injured in an automobile accident in August 1936. He suffered a severe head injury with a depressed frontal skull fracture. He had no further difficulty except for his cosmetic disfigurement for 20 years (fig 1A). On 16 August 1956 a right split thickness iliac bone graft and cranioplasty were performed. The patient has done well and the graft has healed solidly (fig 1B).



Figure 1 (a) (9) (A) Cosmetic deformity that resulted from a automobile accident 1936. (B) Frontal view of the same patient following iliac graft cranioplasty 16 August 1956. The patient is now well healed.

C 10 A 22 year old man suffered a left frontal compound depressed skull fracture on 27 July 1956 in France when he was thrown out of a motor vehicle. The following day an extensive compound depressed skull fracture in the left frontal region was elevated and loose contaminated bone chips which protruded into the brain were removed. A resection of the involved cerebral tissue was carried out and the dural lacerations repaired. The patient had some personality

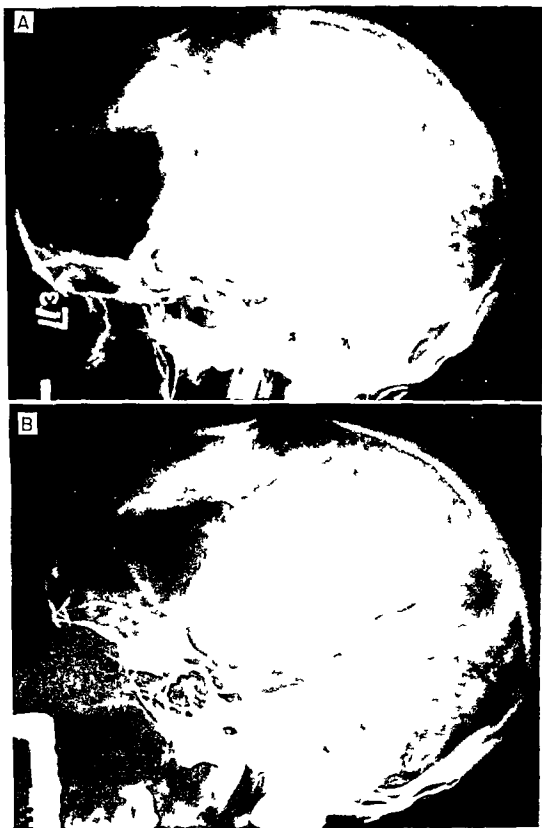


Figure 2 (case 10) (A) Roentgenogram showing cranial defect following the debridement and compression of a compound skull fracture (B) Roentgenogram taken two months after operation, showing bone graft uniting firmly with its recipient bed.

changes when he came to the hospital. These were difficult to evaluate because of alcoholism. His postoperative recovery was complete except for a craniectomy defect (fig 2A). On 21 September a right iliac bone graft was applied to the defect. The patient had an uneventful recovery from this procedure. On 27 November postoperative roentgenograms of the skull showed the graft wedged firmly into place (fig 2B). Follow-up examination on 20 January 1957 revealed no change from the previous examination.

C 11. A 24-year-old man was riding in an automobile that struck a tree. He suffered a large compound depressed skull fracture in the left frontal region. On 9 June 1956 part of his depressed skull fracture was elevated and contaminated fragments were removed. The frontal sinus on the left was obliterated. His postoperative course was uneventful except for a recurrent attack of sinusitis. On 1 August radical frontal and ethmoid sinusotomy was carried out with complete relief of symptoms. On 17 October anterior iliac graft and cranioplasty were performed (figs 3A and 3B). The patient has been asymptomatic. On examination on 20 January 1957 his graft was firmly in place and he was well satisfied with the cosmetic result.



Figure 3 (Case 11) (A) Composite of follow-up compound skull fracture of the left frontal bone (B) Immediate postoperative view of the composite iliac bone graft.

C 12. A 21-year-old man suffered a compound depressed fracture of the right and left frontal bones in an automobile accident. On 6 August 1956 some of the depressed fracture was elevated but much of the contaminated segment had to be removed and both frontal sinuses were obliterated (fig 4A). At the same time a compound fracture of the medial shaft of the left tibia was debrided. On 24 October a full thickness right iliac bone graft was applied to the craniectomy defect. The patient's postoperative course was complicated by thrombophlebitis and a single pulmonary embolus. He was kept on anticoagulants for three weeks even though he was ambulatory. At the end of this time his thrombophlebitis had disappeared and his postoperative course was without further incident. The right orbital ridge protruded too far

over the lateral portion of the skull and on 14 December under local anesthesia the ridge was molded to give a better cosmetic result (fig 4B). When the patient was examined on 11 January 1957 his graft was solid to palpation and the cosmetic result was satisfactory.



Figure 4 (case 12) (A) Marked depression of both frontal bones following a compound depressed fracture in an automobile accident. (B) Contour restored by iliac bone graft cranioplasty.

### DISCUSSION

A historical review of the repair of cranial defects is given in some detail by Grant and Norcross.<sup>2</sup> It seems obvious that the use of autogenous bone grafts to obliterate large cranial defects has been rewarded with a high percentage of successful results. Lambros,<sup>3</sup> in 1943, reported a case in which a large postoperative defect was repaired by a graft from the ilium and discussed the literature on the subject. Even though this case was successful, Lambros believed that there were a number of disadvantages to the method. These included spontaneous fractures of the graft, alteration in gait caused by pain from the donor site, and a "Herculean surgical procedure" to obtain the graft and apply it to the cranial defect. He recommended methyl methacrylate as a substitute for autogenous bone grafts.

McClintock and Dingman advanced a rather convincing argument in favor of autogenous bone grafts, and the points made in their article are ones with which we concur wholeheartedly, based on our own experience. We believe that the removal of the iliac bone graft is a rather minor procedure. In our experience it proved to be traumatic in only one case in which the patient suffered severe hypotension and cardiac arrest, which was quickly reversed with a cardiac pacemaker. This did not result in any neurologic or other deficit to the patient. This particular patient, however, was rather prone to hypotensive episodes. He fainted twice before the operative procedure was carried out, and also had a very low blood pressure after lumbar puncture in preparation for doing a pneumoencephalogram. He required an enormous amount of sedation subsequently when a successful pneumoencephalogram was performed. The operative procedure in which the cardiac arrest occurred was carried out with a minimum of pain-relieving anesthetic agent, as the patient was given a continuous intravenous

drip of a curare like agent. It is possible that he responded in an exaggerated manner to the surgical procedure because in sufficient anesthesia was used

In no case was there an excessive loss of blood during removal of the iliac bone graft. In only one patient was there any incapacity in the patient's gait and this disappeared after the reabsorption of hematoma at the donor site

Satisfactory cosmetic results following this type of cranioplasty were easy to achieve because an abundance of bone could be removed from the ilium and the graft could be molded to the correct contour of the cranium. Furthermore the graft could be shaped so accurately and the craniectomy site could be so well prepared that in many instances the bone graft could be fitted into the cranium and held in place without wires or other retaining materials

There were no postoperative infections in any of our cases even though most of the wounds had been badly contaminated at the time of the original injury and the bone graft in four cases was inserted into the frontal sinus region. Two of these patients showed signs of frontal sinusitis at operation yet the grafts have remained solid and there have been no complications to date. The chance of fracturing a well healed bone graft seems remote. On the other hand a recent report in the literature indicates that large plastic or methyl methacrylate cranioplasty plates sometimes do fracture

We wish to emphasize that this is an initial report on a series of patients who all have had satisfactory results. The longest follow up to date is a year and a half. At the end of a five year period however we intend to question and examine this series of patients and write another communication on the observations to be made at that time

#### SUMMARY

The initial repair of large cranial defects has been accomplished with the use of anterior iliac bone grafts. The initial impression after operating on 12 patients is that this form of bone graft provides a satisfactory structural and cosmetic result

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# CLINICAL EXPERIENCE WITH 682 CASES OF ASIAN INFLUENZA

LAWRENCE S. GREENE *Lieutenant MC USNR*  
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**I**NFLUENZA has affected mankind with varying intensity for many years, but only since the epidemic of 1933, when type A influenza virus was isolated, has this disease yielded to accurate laboratory as well as clinical diagnosis. In April 1957 influenza once again began one of its characteristic peregrinations<sup>1</sup> spreading rapidly from Asia to Europe and the United States and eventually involving most of the world<sup>2,3</sup>. The causative virus of this "Asian influenza" was identified as A/Japan/305/57.

The clinical material herein presented concerns 682 cases of Asian influenza seen during October and November 1957 in an epidemic characterized by sudden dramatic onset in a select population of previously active healthy military personnel.

**Symptoms** The frequency distribution of symptoms encountered in the 651 uncomplicated cases of influenza is charted in figure 1. Considered graphically the symptoms appear to be non-specific but distinct individual characteristics of the following six symptoms were easily discernible and contributed greatly to the facility with which the clinical diagnosis could be made.

*Headache* characteristically dull, severe and unremitting, located frontally or retro-orbitally and often associated with marked somnolence was a frequently repeated complaint.

*Fatigue* overpowering in nature causing healthy young men to become incapable of performing their duties was prominent.

*Cough* typically dry, irritating and not productive of any type of sputum was characteristic.

*Chills* more correctly frank rigors was a dependable, readily recognized symptom.

*Ocular pain* aggravated by any and all motion of the eyes and leading to minimal use of the eyes was an unmistakable finding.

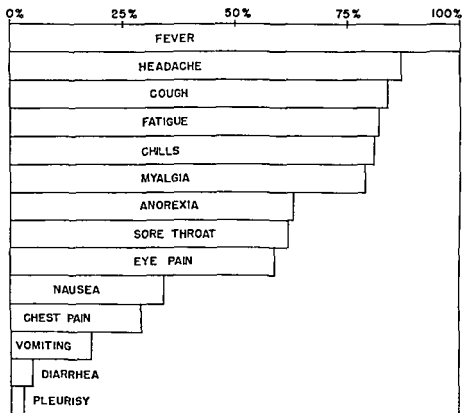


Fig. 1. Frequency distribution of symptoms in 651 patients.

*Myalgia* referred to the low back area was an often repeated complaint of a large number of patients.

In contrast other common symptoms such as soreness of the throat, chest pain, anorexia, nausea, and vomiting, were notably insignificant.

**Physical Examination.** The findings on physical examination of the chest including inspection, palpation, percussion, and auscultation were strikingly negative with a total lack of localizing signs. Very rarely were minor scattered rhonchi, occasional wheezes, and less frequent discrete rales heard. Plethoric facies associated with elevated temperatures were found uniformly. Pharyngeal injection, nonspecific in type and associated with discrete, mobile, slightly tender cervical lymph nodes was common.

**Laboratory Studies.** Laboratory findings were nonspecific and of little diagnostic value. Because of the dramatic acuteness of the epidemic with involvement of a large number of our labo-

ratory personnel bacteriologic studies were of necessity minimal. Hematologic observations revealed normal hemoglobin. The white blood cell count generally was found to be between 5 000 and 9 000 per  $\mu$ l with little in the differential count that varied from normal. No shift to the left was noted; however, a relative lymphocytosis was observed frequently. Urinary abnormalities were infrequent; albuminuria occurred in 3 cases, microscopic hematuria in 8, and microscopic pyuria in 14. Subsequent studies revealed that these abnormalities cleared spontaneously. Roentgenograms of the chest were taken on all patients. Chest films measuring 14 by 17 inches were obtained in 519 cases; the remaining 163 had 70 mm chest films. In uncomplicated cases of influenza the chest films were uniformly normal.

Shortly after the onset of the epidemic blood specimens were drawn from 16 patients including the first 10 seen in order to determine the nature of the afflicting virus. Subsequently when the clinical pattern of the epidemic had become obvious, only 1 patient from each 100 was studied serologically. A four fold or greater increase in antibody titer in the convalescent specimen as compared to the acute stage specimen was considered positive evidence of infection by the agent whose antigen was used in the test. The results of these studies performed by U S Naval Medical Research Unit No 4 Great Lakes Ill indicated that the offending agent was the Asian influenza virus A/Japan/305/57.

**Effect of Vaccination.** Vaccination of local military personnel was begun as soon as the polyvalent vaccine with Asian strain included became available for wide scale use in the area. Personnel were immunized on one occasion by intradermal injection of 0.1 ml in each arm. Of the 682 patients with influenza in this series 376 (55 per cent) had not been immunized, 201 (30 per cent) had been immunized one week before they became ill, and 105 (15 per cent) had been immunized two weeks prior to the onset of illness. There was no discernible difference in clinical picture, complications, or course of the disease between the immunized and nonimmunized groups.

**Temperature Curve.** As shown in figure 2, 91 per cent of our uncomplicated cases had a temperature curve characterized by a progressive downward trend reaching normal levels in 48 to 72 hours without salicylate therapy. This failed to occur in 9 per cent of the cases, being replaced by a persistent febrile response which waxed and waned, finally reaching normal after five to seven days of hospitalization.

**Nature and Frequency of Complications.** As is well recognized, the principal dangers in an influenza epidemic lie in the complicating illnesses. Those that developed in this series are enumerated in table 1.



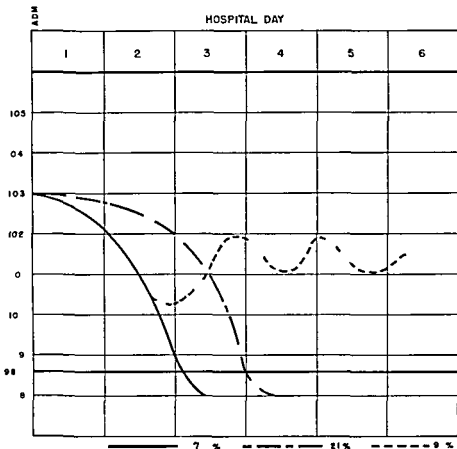


Figure 2 Variation of temperature per group 651 uncomplicated cases of influenza.

TABLE 1 Complications of influenza 68 cases

Complication	Number	Incidence (%)
Bacterial pneumonia	17	25
Otitis media	7	10
Bronchitis	4	6
Sinusitis	3	4

We considered the term complication to imply the development of an illness of the type listed in table 1 after infection with the influenza virus as characterized by the previously described clinical symptoms. The most important clinical aid in

detecting a developing complication was the characteristic temperature response which occurred provided that continuous salicylate therapy was not employed. Every one of the 21 patients in our series who developed a complicating illness failed to become afebrile in 72 hours. Their temperature curves waxed and waned returning toward normal only after six to seven days.

Although this type of response was exactly like that found in 9 per cent of the uncomplicated cases in this series, as shown in figure 2 it provides an urgent clinical warning to the practicing physician. When such a febrile response is encountered, careful re-evaluation of the case with appropriate diagnostic procedures including the necessary radiologic techniques, is in order, to rule out the presence of a complicating infection.

*Therapy and Length of Hospitalization* The principal treatment of uncomplicated cases in this series was bed rest supported by fluids of all types administered by mouth in large quantities. Simple expectorants were used and where indicated mild analgesics and nasal decongestants were employed. Parenteral fluids and alcohol sponging were utilized only for severe febrile responses. With this simple but effective regimen the average hospital stay was six days. Indeed in uncomplicated cases, it was obvious that hospitalization was necessary only as an epidemiologic control measure.

There has been much recent emphasis on the failure of antibiotics to prevent the pulmonary and other complications of viral diseases<sup>4</sup> including poliomyelitis, measles, the common cold, and influenza. Moreover the harm that may arise from widespread use of antibiotics in influenza has been stressed on numerous occasions.<sup>5</sup> It has been shown that despite the total ineffectiveness of antibiotics against the influenza virus they frequently are effective in combating the potentially fatal bacterial complications of the respiratory tract which may result from this disease. However with the routine use of antibiotics prophylactically in such an epidemic the result may be the widespread development of antibiotic resistant infections. Accordingly we used only symptomatic therapy in all cases of this series with the exception of appropriate chemotherapy when a distinct complication attributed to secondary infection occurred.

This clinical study convinced us that complications arising from influenza are easily and accurately recognized by clinical means. Provided sustained antipyretic therapy in the form of salicylates is not employed a characteristic febrile response provides a reliable clue to the presence of a complication. When such a febrile reaction is observed the physician must carefully reappraise the situation and begin a diligent search for the locus

of a secondary infection. Once discovered the complication can be effectively treated.

Of secondary importance inexpensive readily available medications are adequate for successful therapy of influenza without necessitating undue financial strain on the patient.

### SUMMARY

A clinical study was made of 682 cases of influenza seen in a sudden epidemic in a military population and serologically confirmed as caused by the Asian influenza virus. It was found that the disease presented a distinct symptom complex which made possible accurate diagnosis on a clinical basis. Physical and laboratory findings tended to be insignificant in uncomplicated cases. In 91 per cent the temperature decreased steadily to reach normal in 48 to 72 hours but in 9 per cent it fluctuated between 101 and 102 F for several days. Immunization either one or two weeks prior to onset of the illness had no discernible effect on the clinical picture or course of the disease.

Symptomatic treatment without use of antibiotics resulted in rapid recovery with no fatalities. Complications in 4.6 per cent of the cases were successfully treated with antimicrobial agents. In every case in which salicylates were not being used extensively the presence of a complication was heralded by a characteristic fluctuating temperature curve providing a clear warning that search should be made for a possible complication.

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# GROUP THERAPY WITH MEDICAL PATIENTS

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EUNICE L. CUNNINGHAM

**A**T a large military base a shortage of psychiatrists results in a situation where therapy is necessarily minimal. Such a problem exists at this hospital. One psychiatrist and one psychiatric social worker comprise the neuropsychiatric staff with from 35 to 50 admissions to the Psychiatric Service per month, and an average of about 200 consultations each month. The psychiatrist can do little more than categorize and transfer to larger psychiatric units most of the patients in need of therapy.

## PROBLEM

Keenly aware of the need for a psychiatric approach to certain medical problems, several members of the Department of Medicine, together with the psychiatrist and the medical social worker, decided to formulate a more complete therapeutic program for so-called psychosomatic cases. It was apparent that the psychiatrist had little time to participate in the treatment of patients on other services. It also was clear that personnel with little training in psychiatric procedures, especially those related to therapy, would flounder somewhat aimlessly in any psychotherapeutic endeavor undertaken without the guidance of a psychiatrist.

## METHOD OF INDOCTRINATION

Twice a week for six weeks the psychiatrist met with two members of the Department of Medicine and the social worker assigned to their wards for 1½ to 2 hours of indoctrination. The aim of these sessions was to establish certain guides in group therapy. Because only a few ideas could be well established in the limited time the psychiatrist devoted these sessions exclusively to a study of the emotions and in a general way elucidated their manifestations in those suffering from psychosomatic illnesses. Principally stressed in the psychodynamic genesis of these disorders was the *modus operandi* of hostility. An attempt was made to promote insight into the process by which hostility, deviously expressed, is transposed into physical complaints and symptomology. The detection of concealed

hostility was emphasized by study of verbalizations and by observation of attitudes and physiologic responses—postural facial vascular et cetera

To orient those conducting the group sessions and to establish goals in the minds of the patients introductory approaches to group therapy were reviewed and attention was invited to the necessity of promoting an emotional rather than an intellectual atmosphere. The role of the therapist was presented as that of a catalyst accelerating the production of emotional material the expressions of the feelings of disturbed patients. The formulation of meanings in terms of illness and health was to be derived from this material. Principally avoided were the academic formulas of the classical psychiatrists. Jargon such as ego id castration complex Oedipus situation anal oral and similar terminology was rejected assiduously. Family situations were examined especially those in childhood that may have been conducive to the generating of fear with its attending hostility reactions. Attitudes towards one's self and towards others were presented as reflections of feelings promoted in the relationships of the patient to those in authority. These attitudes and their attending affective reactions were illustrated and the chronology of specific cases was used to facilitate emotional understanding.

#### SELECTION OF PATIENTS

Between December 1955 and February 1957 seven psychotherapeutic groups were organized on the Medical Serv. One group consisted of nine mothers of children with enure that was suspected to be of a psychogenic nature. The remaining six groups were made up of a total of 63 patients from two medical wards with various medical illnesses that were considered to be psychosomatic in nature. The diagnoses included peptic ulcer tension headache psychogenic cardiovascular disease neurodermatitis ulcerative colitis rheumatoid arthritis and bronchial asthma. Thirteen of the 63 patients were diagnosed as having peptic ulcer.

The two medical officers selected the patients after completion of medical studies. Only those patients with apparent psychopathology were selected and an attempt was made to eliminate those not considered well motivated to profit by the experience. Ages ranged from 17 to 55 and the average was 28 years. Length of service varied from 6 months to 26 years averaging 6 years. Rate included seaman to chief. Eight of the 63 patients were chiefs and 3 were first class petty officers. A minimal social evaluation of each patient was made by the social worker and presented to the medical officer concerned preliminary to the acceptance of the patient into group therapy.

Each group of medical patients had an average of ten patients. The groups met an average of 11 times in 2 hour sessions twice a week. The leaders were one of the two medical officers and the medical social worker. The group sessions were held in a private office removed from the medical ward. An effort was made to promote an informal and casual atmosphere. In some of the groups new members were added as old members were discharged to duty.

### PROCEDURE AND RESULTS

Ground rules which were established with the idea of making each patient as comfortable as possible, were as follows: (1) rank was not to exist within the group; (2) all material presented was to be considered confidential within the group; (3) each patient was to be privileged to talk or not talk as he pleased, or to come and go as he wished during the sessions; (4) each patient was to be encouraged to express himself as he wished. Throughout the period of the study, the two ward medical officers and the social worker met with the psychiatrist once or twice a week to discuss the emotional situations engendered within each group.

In general the process which evolved in each of these groups followed a similar pattern. Each patient was informed that he had been especially selected for this extra prescription but was privileged to refuse it or to discontinue it at any time. All 63 patients accepted immediately and only 5 discontinued before completion.

During the first meeting the medical officers were asked many questions, and they freely gave medical information in terms that the patients could understand. The doctors and the social worker gave a preliminary explanation of ways in which feelings cause inner tension and the physiological effects were outlined. An effort was made in the initial meeting to convey some meaning to behavioral and emotional patterns. The value of examining our feelings and actions for the express purpose of understanding ourselves was emphasized. This understanding was represented as a means of accepting ourselves thereby experiencing less tension, less anxiety, and therefore less illness.

After the patients had satisfied their curiosity about their particular illness and had gained new knowledge of ways in which they were promoting their illness, they appeared eager to talk about themselves. Items discussed included the patient's interpretation of his illness, his feelings about the treatment, and his explanation of the causes. Attention usually moved to the patient's early life, to the significant figures in his development, and to his feelings toward these persons. After approximately four meetings the patients generally were com-

municating freely with each other agreeing and disagreeing beginning to see in others emotional causes for their illnesses as well as some of their resistances to giving up old habits and emotional patterns After about five sessions many of the patients began to experience a gleam of insight into their difficulties and to express their acceptance of this insight to the group

Gradually the group processes and group feelings changed so that the staff leaders were participating to a minimum Natural leadership within the group began to take over the direction the patients showing less concern over what the staff leaders and other members thought of them as they began to operate more openly in their verbal and nonverbal communication Friendships were established and the group-communications continued in smaller groups on the wards Feelings of responsibility to each other began to emerge and self understanding from an emotional viewpoint commenced to gain stature as a goal in the approach to emotional and physical health

During this group process patients were observed to become comfortable enough within the structure of the group to express their fears of making mistakes their feelings of being mistreated whenever reprimanded their exaggerated suspiciousness and their feelings of failure worthlessness and lack of self esteem These expressions promoted awareness of kindred patterns of emotional reaction in the lives of each of us Slowly but definitely a sense of humor began to permeate and above all a degree of self acceptance

It is interesting to note that the basic philosophy of social work was brought into operation within the groups This philosophy includes belief in the basic worth and dignity of each person the right of self determination the importance of non judgmental attitudes and the ability for change and growth inherent within everyone The tone of meeting after meeting expressed this basic thinking and was reflected in remarks heard first from the group leaders and quickly picked up and used constantly by the patients about themselves and others—such remarks as "It's O.K. to be human you know Why can't you forgive yourself? Why do you have to be always perfect?" "It's all right to be all wrong at times"

Hostility and resistance were more apparent in the early meetings and were encountered usually in the form of skepticism disbelief doubt silence et cetera Such statements as "This stuff is a lot of bunk What has my childhood got to do with my headaches? How are you gonna talk me out of my stomachache?" are examples of these reactions

Some patients experienced immediate and dramatic relief from anxiety during the group process For example a Negro

who had suffered with asthma nightly for four months, and who came to his first meeting in a wheelchair, breathing heavily, became completely asthma free while ventilating extreme hostility towards recent authority. He was given support by the medical officer as well as by the group members. He remained asthma free for the following four weeks in the hospital. Another patient with tension headache was amazed by his feelings of relief, after ventilating the hostility he had experienced in childhood towards his step father, concomitantly with his expressions of hatred towards his commanding officer.

It is interesting to note that the majority of these 63 patients expressed positive feelings toward mother, and negative towards father. In fact more than 40 of the group openly expressed resentment, anger and fear in re-experiencing their feelings of being unfairly and oftentimes abusively treated by their male parent. Many patients were able to help others relate their present reaction to authority to the early emotional patterns of childhood. As an illustration, one patient was admitted to the hospital with hypertension of a degree that made it impossible for him to re-enlist. He was able in group therapy to associate a recent reaction to a reprimand from his commanding officer to his extreme fear and hatred of his father as a child. The commanding officer had called the serviceman to his office a few days prior to his re-enlistment time and had talked to him about an outstanding bill long overdue. The serviceman had planned to use his re-enlistment money to pay off the bill and other accumulated obligations. In group sessions this young man was supported by other members and encouraged to talk about himself. He poured out long repressed feelings of resentment toward his father who had left his mother while the serviceman was a child, with resulting financial deprivation to himself and his siblings. With some direction from the group, he began to understand the relationship between his earlier emotional reaction to his step father and the present disproportionate reaction to his commanding officer's reprimand. His blood pressure began to improve and eventually he was able to pass his physical examination for re-enlistment.

Another patient, a 17 year old seaman, was admitted to the hospital with tension headaches. He had been in the service for seven months. He told of being the oldest child in a large family. His father was described as erratic and the patient expressed feelings of great concern over the welfare of his mother and younger siblings. He dreamed of his mother almost nightly. As he talked, members of the group began to see the connection between his anxiety about getting out of the service to help his family and the feelings of inadequacy he had experienced in his earlier home environment. He told of repeated



incidents in the service of his feelings of being picked on because he was the smallest man in his outfit as well as the lowest in rate. In subsequent group meetings he was placed affectionately in the role of the kid brother of the group. He began to feel a sense of union with the other members and to experience a feeling of security in this situation. He began to appreciate the value to his own personal growth and development of remaining in the service of learning to adjust to life away from his mother and of experiencing satisfying relationships and accomplishments which are possible in the Navy. He finally expressed the fact that it was quite possible that he could help his mother more financially by remaining in the service than by going home. He discontinued to dream of his mother and his headaches went away. He asked his doctor, the co leader of the group, to return him to duty and to help him get back to his former duty station.

Of the 63 patients only 5 discontinued attending the group prior to its completion or their discharge from the hospital. A total of 54 patients reached a mutual decision as to their return to active duty and one of the requisites for return to duty was improvement in symptomology to warrant a designation "fit for duty." The number of patients discharged from military service during this period of group therapy was markedly diminished on the two medical wards involved. Treatment of these medical patients by means of group communication was the only change that had occurred during this period.

The seventh group conducted during this period concerned a group of 9 mothers with children suffering from enuresis for which no organic basis could be found. Each child was given neurologic and electroencephalographic examinations by the psychiatrist. Following the medical work up the mother was referred to the social worker for an individual social study before she was added to the group. In addition to the 9 children with enuresis these 9 families included 20 other children, some of whom suffered from stuttering, eating difficulties, sleeping irregularities and behavior disturbances. The mothers ranged in age from 21 to 35. The group sessions were conducted by the two medical officers and the medical social worker who had worked with the medical groups. Again they acted as co leaders.

A form was given to each mother in the last session or tenth meeting in an effort to measure the results. Information on these forms, which were mailed back to the social worker, indicated that every one of the enuretic children had shown improvement, several becoming dry at night for the first time. Plans have been made to have follow up meetings with this group of mothers to ascertain if the initial improvement is sustained. A check on the outpatient charts shows a decided decrease in clinic visits following this period of group therapy for these families.

## SUMMARY AND CONCLUSIONS

A program has been outlined whereby a psychiatrist has utilized nonpsychiatric personnel in a group therapy program involving medical patients. During the therapy these patients at no time were under the direct observation of the psychiatrist. The two medical officers and the social worker leading the group sessions were given a specific type of indoctrination by the psychiatrist, who then met with them biweekly to evaluate the emotional material produced in the group relationships. The following conclusions were reached as a result of this study.

1 The function of a psychiatrist in a general hospital can be greatly enhanced by assimilating nonpsychiatric personnel into a therapeutic program that involves other than patients under his direct supervision.

2 It is possible by brief but adequate indoctrination for medical and associated workers to conduct effective group therapy with psychosomatic patients.

3 Group therapy by nonpsychiatric personnel must be continuously under the guidance of a psychiatrist.

4 Medical men regardless of specialty may utilize to the advantage of their patients the techniques of group therapy in a controlled situation.

5 The group communication method is an effective one for bringing together quickly easily and naturally the medical, psychological and social factors of individual cases.

6 The morale of a medical ward improves when group therapy is utilized.

7 Patients who participate in group therapy probably experience a more lasting recovery than would be possible by the use of medications alone.

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ACKNOWLEDGMENT The authors are grateful to Lt C mdr Woodrow B. Tren MC USNR and Lt C mdr Leo Nastasi MC USNR for their active participation in this study.

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## NEW ASSISTANT FOR DENTAL SERVICES USAF

Brigadier General James S. Cathroe USAF (DC) has been appointed Assistant for Dental Services to succeed Major General Marvin E. Kennebeck USAF (DC) who retired on 31 January 1958 after more than 33 years of service. It was announced by Major General Dan C. Ogle USAF Surgeon General.

A native of Omaha, Nebraska, General Cathroe received his Doctor of Dental Surgery degree from Creighton University Dental School in 1928. He entered on active duty with the Army that year and served his internship at Letterman General Hospital, San Francisco, California.

General Cathroe transferred to the Air Force in July 1949 where his assignments have included duty as Command Dental Surgeon of Eastern Flying Training Command, Caribbean Air Command, and Air Training Command. He was appointed Deputy Assistant for Dental Services in 1955.



General Cathroe

General Cathroe is a member of the American Dental Association and the *Fédération Dentaire Internationale*.

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## World Health Day

The traditional date of World Health Day, 7 April, will mark the tenth anniversary of the World Health Organization. This day should serve to review and publicize the strides made toward the WHO goal—the highest possible level of health—which has been achieved during the past decade of national and international effort made possible through the cooperation of local, national, regional, and international health organizations.

These achievements—in the form of new technical means, intensified educational programs, improved health legislation, and expanded facilities for the rapid exchange of medical information—are the substance of a collection of articles published by the WHO heralding Ten Years of Health Progress.

Future issues of the *U.S. Armed Forces Medical Journal* will reproduce important parts of the articles that are considered of paramount interest to our readers.



## Clinicopathologic Conference

U S Air Force Hospital Wright Patterson Air Force Base Ohio

### FATIGUE

**Summary of Clinical History** Approximately 1 to 2 years before admission, the patient, a 73 year old woman, noted the onset of increasing exertional dyspnea fatigability brownish pigmentation and dryness of the skin, epilation, progressive bilateral deafness stiffness of the neck and elbows and intermittent anorexia. She was first seen by a physician about 9 months before admission complaining of hearing loss pruritus ani, and fatigue with vague complaints of nocturia and edema during the previous year. She recalled having been told that her blood pressure was elevated 25 years before this visit. Physical examination now showed a pressure of 200/110 mm Hg. She was treated with rauwolfia. Within one month she noted vitiligo and progressive edema particularly involving the face periorbital tissue and head. This was diagnosed as hives and treated with anti-histamines. The patient's blood pressure was then 170/90 mm Hg. A few weeks later she consulted her physician because of marked cyanosis pain and ulceration in her finger tips. She was treated with Priscoline (brand of tolazoline hydrochloride) and in two months the fingers healed.

Four months before admission she was observed to have 3 plus edema of the legs with a blood pressure of 140/70 mm Hg. She complained of generalized aching and stiffness diagnosed as "flu" for which she was given an injection. The aching and stiffness persisted, however. Urinalysis showed a trace of albumin and a few white blood cells. Sedimentation rate was 40 mm

Roentgenograms revealed some osteoporosis which is probably related to her age as is the arthritis and the pruritus and Intermittent anorexia is often due to azotemia which in turn is present in certain kidney diseases one of which I believe this patient had

The physical examination states that the patient was well nourished but there was no comment on the severity frequency or duration of her intermittent anorexia It did comment that she had lost no weight recently I assume that the statement well nourished would be in keeping with her age Except for one reading of 140/70 the blood pressure was consistently elevated both by history and on physical examination The pitting edema was certainly significant suggesting some recent cardiac failure The only comment on the retinal examination was that she had minimal arteriovenous nicking A 73 year old woman with a 25 year history of hypertension and only arteriovenous nicking probably had intermittent hypertension I assume she had normal neurological findings

There were gaps in the history one was that on the initial examination there was no comment on the physical findings in her chest With what appears to be a moderate amount of congestive failure there should be some findings There were no comment on the heart sounds A roentgenogram revealed moderate cardiac enlargement I would expect some murmurs if only functional ones There were no comments on the condition of the vascular system The fact that she had ulcerations on the tips of her fingers some months before and that they had healed with Priscoline treatment suggests some kind of vascular spastic disease There was no comment on whether she had peripheral arteries the condition of the brachial or radial pulsation

The laboratory features reveal a little more of the situation with which we are dealing The low specific gravity of the urine (two readings of 1.010 and a reading of 1.012) suggests marked loss of ability to concentrate the urine This would be consistent with some sort of nephritis Microscopic hematuria and white blood cells were noted in the urine as well as albumin and casts The hemoglobin of 10.5 grams represents a slight anemia consistent with the general illness found in these nephritic conditions Her blood urea nitrogen was elevated to 45 mg per 100 ml Doctor Sillman stated that a previous reading was lower than this indicating progressive accumulation of nitrogenous waste products The depressed serum calcium and the elevated phosphorus are consistent with nephritis

In elderly patients persistent sinus tachycardia as shown in the electrocardiogram may be evidence of coronary disease of long standing The total protein was low with inversion of her albumin globulin ratio This doesn't seem to fit the diagnosis which I had in mind however I don't think its being the case will necessarily rule out the conclusion During her hospital course she developed a mild fever which might well be attributed to a developing pneumonia I recall no other indication of an infectious process The protocol mentions severe ab

dominal pains In reviewing the literature I found something that I have never seen but have heard about that is angina abdominis This is a condition of abdominal pain apparently very similar physiologically to angina pectoris Angina abdominis is generally relieved with mild narcotics and sedation These drugs relieved the patient which supports this hypothesis

In summary this patient had hypertension on admission and probably had had it for a long time She had nephritis and probably coronary insufficiency Hypertensive cardiovascular disease is common in people of this age The one diagnosis that seems to tie all these things together is an arteriolonephrosclerosis The finding against it is that the patient had edema and the disease is a chronic non edematous form of Bright's disease The patient may have had a chronic nonedematous form with edema due almost solely to cardiac failure rather than the nephrosclerosis This is the diagnosis I offer—arteriolonephrosclerosis with the other changes due to senility Possibly she died of the uremia maybe she had a pneumonia

Doctor Sillman Thank you Doctor Claro In looking over the chart there were two blood urea nitrogen tests recorded The first on about her third hospital day was 25 and the second (and last) on about the eighth day was up to 45 mg per 100 ml She died about five days after that Her urine output was rather small averaging 200 to 400 ml Before we go any further could we see the roentgenograms Doctor Watts?

Doctor Watts Most of the time the sicker the patient the poorer the films It is true in this case The first two films were made I assume before the patient became ill They reveal an enlarged heart the configuration indicative of left ventricular enlargement There is no pulmonary congestion at this time Could I find out when she became ill?

Doctor Sillman About one and one half to two years ago The symptoms before that were quite vague—present perhaps for another year

Doctor Watts Now we come to portable studies which were made when she was acutely ill—notice the heart has increased in size Much of the apparent heart enlargement may be due to the fact that these are portable films There is no date on any of the portable studies Now notice her lung picture She had definite pulmonary congestion The pulmonary vessels are fuzzy indicating pulmonary edema especially marked in the right base The interlobar fissure is thickened The next film shows essentially the same findings In our last film the edema is more pronounced (fig 1) She had edema of the left lung also plus pulmonary congestion We have a single film of the abdomen which technically is very poor I see no pathologic condition except the asymmetry of the pelvis which may have been due to an old injury There are some mottled areas of increased density in both upper

quadrants which I assume are artifacts. I think the roentgenograms indicate hypertensive cardiovascular disease with congestive failure, pulmonary edema, and in one film radiolucency in the left base that could be caused by a pulmonary embolus.



Fig. 1. Postero-anterior and lateral roentgenograms of the chest showing congestive failure and pulmonary edema.

Dr. Sillman: In regard to the pelvis, this patient was in an automobile accident several years ago. Dr. Tobin will you please discuss the case?

Dr. Tobin: When one reads this case, it seems to be that of an old lady who had had hypertension for years, developed heart failure and renal failure, had terminal bronchopneumonia, and died of an acute complication, such as a perforated ulcer. But this is too obvious to be a Clinical Pathologic Conference material. It omits such things as the known pigmentation, which is mentioned in the protocol.

several times. The patient had stiff elbows—really stiff because she had contractures meaning trouble for a long time. She had periorbital edema, edema of the scalp, and complained about vertigo. Her sedimentation rate was elevated. She had increased serum globulin, decreased albumin, and she had gastrointestinal symptoms.

Now, in young people we try to fit everything we can into one diagnosis, but in the old we can often find two or more diseases; however, even in the old it is good practice to reduce the diagnoses to a minimum. The variety of complaints and the findings which were left out of the first explanation should be fitted in in some way. To go over them again, we have evidence of disease of the cardiorenal systems, the joints, the blood vessels, the skin, the lungs, and the bowels—a really generalized disease. I believe I can explain all of the symptoms on the basis of one collagen disease.

Collagen diseases are strange. They vary so much in their clinical pictures and each one can involve so many systems of the body that one can't easily sort them out clinically. The group includes periarteritis nodosa, systemic lupus erythematosus, rheumatic fever, rheumatoid arthritis, dermatomyositis, and scleroderma.

The widest variety of symptoms seems to occur in periarteritis and lupus. The two diseases can occur at any age, but periarteritis is much more common in men in the 20 to 40 year old group. Systemic lupus is likely to occur in women in the 15 to 35 year old group, but both have occurred from infancy to advanced age. These diseases have been known for a long time. I would like to read you a paragraph Osler wrote in 1895 about disseminated lupus erythematosus which in his day was called something a little different:

By exudative erythema is understood the disease of unknown etiology with polymorphic skin lesions, hyperemia, edema, and hemorrhagic arthritis occasionally, and a variable number of visceral manifestations of which the most important are gastrointestinal crises, endocarditis, pericarditis, acute nephritis, and hemorrhage from mucosal surfaces. Recurrence is a special feature of the disease and attacks may come on month after month or even throughout a long period of years. The attacks may not be characterized by skin manifestations.<sup>1</sup>

This description has been gradually amplified. In 1904 the description of frequent joint involvement was noted<sup>2</sup> as well as pericarditis, pruritus, and kidney disorders, and the constitutional manifestations of fever and prostration. In 1920 leukopenia and thrombocytopenia<sup>3</sup> were noted, and in 1924 Libman and Sachs<sup>4</sup> wrote about endocarditis. Nothing more was added until 1935 when the wire loop lesion in the kidney (a hyaline thickening of the glomerular tufts) was described. In 1948 a real contribution was made by Hargraves and associates who described the LE cell.



Now to get back to this particular case—I can give an equally good argument for periarteritis nodosa or systemic lupus not the type of periarteritis resembling a hyperallergic response but the type that seems to occur occasionally with hypertension and severe kidney damage. Sometimes one can distinguish these two diseases clinically the pathologist often has to make the diagnosis. As I told you periarteritis is more common in men and disseminated lupus is more common in women for that reason I chose systemic lupus for the diagnosis. The cause of collagen diseases isn't really known. Such things as stress from infection exposure to sunlight and cold trauma and allergic reaction to therapeutic agents like sulfa drug and penicillin are perhaps not as much a cause as a trigger mechanism which sets off some underlying disturbance that nobody really understands.

This patient had many complaints in the previous two years. When I read them over it seemed to be the way I also might feel at 73—a case of generalized misery. The brown pigmentation of the arms deserves special notice because in lupus you get in areas that are exposed to sunlight reddish macular lesions such as the familiar butterfly rash on the face. After these lesions heal a dark pigment remains. This is a spotty affair. In this case pigmentation on the arms I imagine was fairly generalized but irregular leaving certain areas of normal skin which might be interpreted as vitiligo. She complained of nocturia which in view of the low specific gravity of the urine indicated loss of concentration and the normal day night ratio of urine output. The edema of the face periorbital region and of the head is interesting. It is not due to kidney or heart failure—not in the right spot. Her doctor treated it as an allergic disorder and gave her antihistamines. There must have been something about it that suggested urticaria. In collagen diseases this type of edema might be expected.

Raynaud's phenomenon was experienced by the patient. This occurs in both periarteritis and systemic lupus. The extent of the phenomenon that this woman had was characterized by general aching and stiffness. She had previous history of trouble with her elbows. In lupus about 70 per cent of the people have arthritis. At least once she had normal urine. A second specimen was slightly abnormal then it became very abnormal. This variation too is found in lupus which tends to alternately be mild or get worse. Her sedimentation rate was high which relates to the change in albumin globulin ratio as found in lupus too.

Her next difficulty seems to be related to renal failure. Her blood pressure rose and she excreted albumin and red and white blood cells. She developed a low grade fever. In this disease she should have had bouts of fever from time to time. The roentgenogram of the chest made when she came to the hospital shows some pulmonary fibrosis and emphysema and not too great cardiac enlargement. Her history states she married hypertension 25 years ago which was when he was about 50 years old. We seem to be able to get along with essential

hypertension for years without much deterioration. It is possible but not very probable that this hypertension was related to lupus. She should have developed other things in the interval that would fit in with lupus. Lupus is a chronic disease but I believe hers started 2 or 3 years before not 25.

Quite a bit of unsuspected pulmonary change can be discovered at autopsy. Nobody pays much attention to this part of the disease because examination of the lungs may reveal a few rales and only little change in the percussion note. There is little evidence of pathology on roentgenograms and yet the lungs are often involved. These patients do show poor pulmonary function as revealed by function studies. I feel sure this patient will show pathologic changes in the lungs. Many lupus patients have pericarditis or recurrent pleurisy, neither of which were seen here. The roentgenograms of the joints don't show changes comparable with her joint symptoms. Hers show osteoporosis but this can be explained by age. Severe joint changes may occur that look like rheumatoid arthritis but on the other hand have very little you can see on a roentgenogram and yet the patient complains of severe pain and there may be joint swelling.

The patient's urine showed marked changes in the kidney function. She was able to concentrate up to 1012 and had an elevated blood urea nitrogen. The hemoglobin was reduced, the hematocrit was 31. This was a moderate anemia which would be consistent with this diagnosis. The white blood cell count isn't so consistent. It was elevated. Usually in this disease leukopenia is present. The electrocardiogram showed nonspecific abnormalities. Myocarditis is another feature of disseminated lupus that may not show much abnormality in an electrocardiogram and still be extensive in the heart. She had no murmurs at all. In Libman-Sachs disease you are going to get at least a systolic murmur somewhere. I attach no significance to the serum calcium and phosphorus determination.

On the fourth hospital day the patient complained of aching in the maxillary sinus, stomach discomfort and shortness of breath. I can't explain the sinus pain except on the basis of mucosal edema. Heart failure patients often have a distended stomach and shortness of breath and discomfort results. To get back to my favored diagnosis, gastrointestinal symptoms are common in disseminated lupus. The lesion is edema and vascular damage that may progress to ulceration and bleeding into the bowel and occasionally perforation. One can also get edema of the common duct ending in pancreatitis.

Something new and sudden happened which precipitated death. She was getting along fairly well when she developed sudden pain, breathlessness and cold sweats. The pain began at the umbilicus and moved down to the pubis. She improved and had two recurrences—possibly a dissecting aneurysm—the pain moving as it advanced. Or she possibly had a ruptured viscus. The trouble with that is that she got along for seven days without showing signs of peritonitis. She was taking

cortisone which might mask symptoms of a ruptured viscus. Then on the day before she died she developed a watery diarrhea which was thought to be caused by Terramycin. That could be true but she had taken antibiotics only six days. It occurs to me that people get diarrhea from antibiotics with a few doses or after a long period of taking them. This was an in-between period. I think it can be explained as a manifestation of lupus. I do not believe an LE slide was made on this patient. Has anybody a question?

A Phy i i: Would you say that the roentgenograms are compatible with collagen disease?

D t: Watt: They are compatible but not diagnostic.

Doct M h i i: I would like to go along with collagen disease. When I was a resident I saw a patient whose illness was very similar to this and which the pathologist diagnosed as scleroderma so I would like to suggest scleroderma.

D t: T b: Clinically the symptoms of these diseases overlap a great deal. In scleroderma one should have very definite skin changes. The skin gets hard, bumpy, waxy and pitted. In dermatomyositis you get skin changes, also muscle changes and muscle pain. Because these findings weren't emphasized in the protocol I chose disseminated lupus.

A Phy i i: Why do you suppose she had a long history of hypertension?

D t: T b: The easiest explanation is to say it was a labile essential hypertension not related to her final illness.

D t: L g: In reading up on this I selected three or four diseases—periarteritis lupus, scleroderma and dermatomyositis. Scleroderma seemed to fit a little closer than disseminated lupus so I would like to put in another vote for scleroderma.

D t: T b: I forgot to mention that in scleroderma you can get arthritic changes too.

Doct L g: Concerning the terminal event I thought of ruptured ulcer particularly in a patient on cortisone and dissecting aneurysm but I also would like to vote for mesenteric thrombosis, myocardial infarction, pulmonary embolus and congestive heart failure.

D t: T b: I interpreted the shadow at the left base as terminal bronchopneumonia rather than pulmonary embolism. The patient should have had differential symptoms from an embolus. I chose dissecting aneurysm because the pain of perforation of the bowel might have been masked by the cortisone treatment.

A Phy i i: Don't discuss ectopic aneurysms causing pain in the back?

Doctor Tobin If they start higher I think they do I believe this one started in the abdomen and dissected down

Dr Claro's diagnosis

Arteriolonephrosclerosis

Dr Tobin's diagnosis

Disseminated lupus erythematosus

### PATHOLOGIC FINDINGS

Doctor Sillman I think you all did well This woman had a collagen disease but it was scleroderma with cardiac fibrosis and pulmonary fibrosis She had benign nephrosclerosis with superimposed malignant nephrosclerosis She had a dissecting abdominal aortic aneurysm Beside that, there was fluid in the chest and abdomen and a few polyps in the large bowel

Going over the gross autopsy findings rather rapidly she had a light brown pigmentation that was mentioned The heart weighed 525 grams and there was evidence of scarring on the gross specimen Each pleural space contained 800 ml of fluid The abdomen held 300 ml of fluid The kidneys weighed approximately 200 grams each and showed some slightly discolored flecks The aorta showed dissection extending about 20 cm but only about 50 ml of blood had actually been extravasated so this accounted for the pain but in itself did not cause death The brain was not examined

Scleroderma is widespread in the body involving not just the skin but often the heart lungs and gastrointestinal tract as well as muscle mucous membrane and kidney The skin is however the classical site Its pathologic condition can be divided into three stages the early brawny edema beginning usually on the extremities the face neck or head the smooth waxy stage and finally the brown atrophic deeply adherent stage The prodromal symptoms are interesting Patients frequently have the weakness and fatigue of which this woman complained sometimes weight loss occasionally fever joint pains or joint stiffness Raynaud's phenomenon is quite common as a prodrome in scleroderma In one group of 15 patients 12 of them had Raynaud's phenomenon There is loss of hair and pruritus Cardiorespiratory symptoms are not too rare They may be early before you see anything diagnostic The patients may have heart murmurs and enlarged hearts rates and electrocardiograms with nonspecific changes

The laboratory findings are not particularly diagnostic A mild anemia elevated sedimentation rate and sometimes reversal of the albumin globulin ratio The urine as in this case shows red and white blood cells and casts Roentgenographic studies may reveal osteoporosis as in this patient or gastrointestinal tract involvement which was not present in this case and often linear or nodular markings in the lung Fifty per cent of the patients in one series showed these lung changes

The slides in this case showed first some edema of the skin with dense collagen fibers (fig 2) The dermis is fairly solid with fibrotic tissue and the epidermis is markedly atrophied (fig 3) The skin appendages are sparse except for sweat glands For some reason they seem to remain Looking at the epidermis a little closer one can see that the dermal papillae are still there in severe cases the papillae flatten out but one doesn't see skin appendages very often in this slide

We have no slide of the gastrointestinal tract there If it is involved symptoms such as difficulty in swallowing nausea vomiting and diarrhea or constipation may occur The usual finding in the heart is fibrosis This patient had a small amount of fibrosis The lung can show fibrosis with or without cystic changes The alveolar walls of the lung in this patient are thickened not markedly so but probably enough to explain her symptoms

The kidney changes are interesting A scleroderma kidney has been described that is so like malignant nephrosclerosis it is difficult to tell them apart The only difference reported is the thickening of the arterioles which show a gelatinous or mucoid change This is a very rare finding in a rare disease The kidney in this patient shows thickening of the arterioles fibrinoid degeneration of the efferent arterioles and hyaline changes Here is a classical glomerulus (fig 4) showing the changes of malignant nephrosclerosis with fibrinoid change involving an efferent arteriole going into the glomerular arterioles as also described in a scleroderma kidney The pancreas and spleen showed some fibrinoid changes in the arterioles

In scleroderma a certain percentage of patients get malignant hypertension—about 3 out of 10 These become uremic in a very short time It had been suggested that treatment with ACTH and cortisone precipitated the malignant phase Inasmuch as it occurs suddenly anyway this is still theory In scleroderma death is usually a result of intercurrent infection because the patient becomes weak and emaciated When the patient develops severe hypertension the causes of death are similar to those of malignant hypertension a cerebrovascular accident heart failure or uremia In this patient there also was a small pulmonary embolus on the left side which had not caused an infarct

As the brain was not examined we can only speculate on the cause of death The dissecting aneurysm could have contributed to the renal damage by period of shock There may have been some uremia but this cannot be proved as there was no recent determination of blood urea nitrogen There was heart failure as indicated among other things by the large amount of pleural fluid and there may have been cerebral changes Are there any questions?

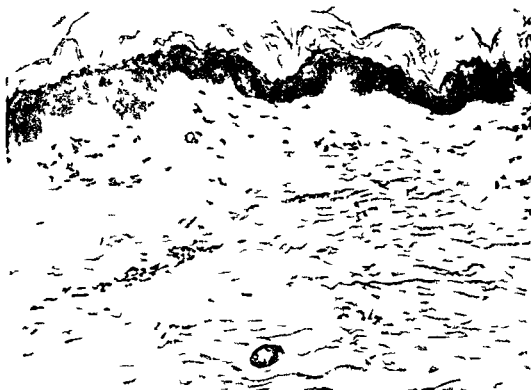
D I G

What about the bowels?

M J Harry C G J USAF (MC) Chief Surg IS em



*Figure 2 High-power view of dermis from right center portion of the section in figure 3 showing dense collagenous fibers (x 525)*



*Figure 3 Section of skin showing dense collagenous fibers fibrotic tissue and atrophy of epidermis (x 195)*

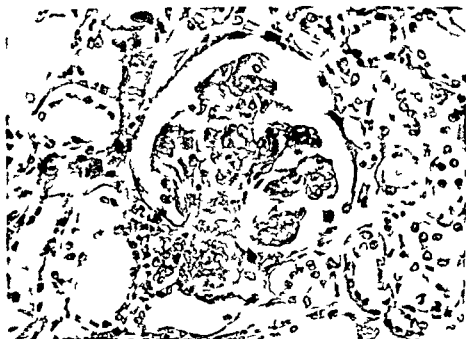


Fig. 4. Section of kidney showing glomerular capillary of afferent arteriole extending to glomerular capillary ( $\times 305$ )

Dr. Sillm. The bowel showed nothing unusual. It was examined carefully. There was no unusual amount of fibrosis at least in the areas of which we have sections.

#### Pathologic diagnoses

- 1 Scleroderma with cardiac and pulmonary fibrosis
- 2 Nephrosclerosis benign with superimposed malignant nephrosclerosis
- 3 Dissecting abdominal aortic aneurysm

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## SERVICE ARTICLE

# THE BASIS OF EFFECTIVE VECTOR CONTROL

VERNON J TIPTON *Captain MSC USA*

**O**BJECTIVE self appraisal is one of the least traveled paths to progress and yet, organizations as well as individuals may experience some stimulation for improvement by a "look in the mirror." This is particularly true of that part of the post preventive medicine program which deals with insects and rodents as vectors of disease. A military installation with conditions that allow insects to breed freely is a mirror that reflects apathy toward the disease potential inherent in large populations of flies and mosquitoes.

In a military organization, a sentry found sleeping on watch merits the court martial that usually ensues. Apathy toward a disease noted for its prolonged absence in epidemic proportions is similarly dangerous, even though an "at ease" posture may seem justified. Unfortunately diseases transmitted by arthropods are characterized by a tendency to promote such apathy.

As late as 1947 there were more than 50 000 deaths in one Indian state from plague alone. In continental United States during the years 1952-1956, the median annual number of cases of malaria was 715. In 1957, up to 20 July, there were 66 cases of endemic typhus and 823 cases of infectious encephalitis.<sup>1</sup> Among military personnel in the Fifth U. S. Army Area during 1956 there were at least 5 cases of tularemia, as evidenced serologically by increased titers, and in 1957 there were several additional cases, one of which has been definitely associated with the bite of a tick.<sup>2</sup> These occurrences lend substance to the very real disease potential presented by arthropod vectors.

### BASIC CONSIDERATIONS

There are some basic considerations of utmost importance in the vector control program which must be oriented properly. They should be viewed with a perspective that takes into account the array of problems confronting the Post Commander, the Post Surgeon, and the Post Engineer.

**Recognition of Problem.** Recognizing that an actual or potential breeding site for insects and rodents does exist is the first mark



of progress in vector control. Realistically there are obstacles in the form of financing, manpower shortages and equipment inadequacies that make progress difficult. The insect and rodent control program however should not be an isolated endeavor standing apart from all other post activities. It should be an integral part of planning so that various phases of beautification and maintenance may accomplish the aims of preventive medicine which then becomes an adjunct to esthetics and economy. Chandler quoted M. C. Hall as saying the louse had its welfare imperiled when the Saturday night bath supplanted occasional immersion from falling into water. The housefly got a severe setback when the automobile replaced the horse. It would be ridiculous to suppose that these two social innovations were instituted for the control of the louse and the housefly but the effect was the same. The tools of preventive medicine are often found under guise and the ability to recognize fortuitous circumstances as allies and to enlist them in the cause is the mark of an experienced Preventive Medicine Officer.

**Importance of Basic Sanitation** The results of the use of DDT for the control of typhus in Naples in 1943-1944 were dramatic but not without perverse effect. To many the advent of DDT and related insecticides heralded a new era in the realm of insect control; however past experience as well as recent investigations furnish substantial evidence that basic sanitation will never yield to chemicals its rightful position in the control of disease vectors. In certain situations it appears that flies are capable of producing more offspring in the presence of larvicides than where no chemicals have been applied and the development of resistance to insecticides may be accelerated or augmented by larvicides. Nothing is changed on a permanent basis by the use of chemicals as a control measure whereas application of the principles of practical ecology (i. e. filling ponds where mosquitoes are breeding and clearing debris from drainage ditches) proves not only more effective but obviates any need for repetition. Good housekeeping practices are still the first line of defense against insect pests and vectors.

**Control With Chemicals** Chemicals play an important role in the control of vectors but must be secondary to the methods mentioned above. The effectiveness of chemical control is largely dependent on application technique. These may be made more efficient by selective use of the chemical based on a knowledge of breeding habits and life histories.

**Identification of Vectors** An effective control program is contingent on the collection and identification of insect and rodent vectors. The direction of the attack is dictated by the information on life history that is corollary to identification. Army medical laboratories are prepared to identify specimens and specific

instructions concerned with collection and shipment of insects are furnished by each laboratory

**Community Education** Perhaps no other field of medical endeavor so involves lay participation as does preventive medicine. Each member of the Armed Forces and his dependents should be conscious of their role in the prevention of disease in the community. Various educational media may be employed in appraising them of their responsibilities. Community education completes the fundamental triad of good housekeeping, chemical control, and an informed public.

**Co-ordination** The Post Surgeon and the Post Engineer are the Post Commander's right and left hands. In this situation it is imperative that the right hand should know what the left hand is doing. Close co-ordination between the Post Engineer and the Post Surgeon is essential if progressive steps are to be made toward producing a vector free environment for troops and dependents.

In all of these considerations, individual responsibilities are only inferred, but most military personnel are aware of specific regulations defining responsibilities that pertain to them individually. Many are the instances where there is a wide gulf between knowing responsibilities and having the wherewithal to accomplish the mission. The support of the Commanding Officer in designating a cleanup day could be a useful tool in this instance. A maximum effort in manpower and equipment directed toward the clearance of unsightly or undesirable conditions on the post would lend great support to the engineer maintenance program while reducing insect and rodent breeding areas. Other types of "do-it-yourself" projects, well organized on a company or battalion level, could produce some very worthwhile results.

#### SUMMARY

Critical appraisal of the post vector control program at frequent intervals is essential in view of the dangerous apathy likely to prevail. Effective control depends on (1) integrating the control program into post beautification and maintenance activities, (2) directing the major effort toward basic sanitation and good housekeeping measures, especially those having a permanent effect, (3) using chemical control only as secondary to basic sanitation, (4) collecting and identifying all vectors, and directing attack in accordance with breeding habits and life histories, (5) educating military personnel and dependents as to their responsibility in the control program, and (6) obtaining both the support of the Post Commander and co-ordinated action by the Post Surgeon and Post Engineer.

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## MISSILE TYPE INJURIES FROM ROTARY LAWNMOWERS

The introduction of any mechanical labor saving device into routine life may hold unsuspected danger for its users. In recent years the efficiency of the rotary power lawnmower has been recognized widely. This mower has enjoyed increasing sales and popularity and its use is now quite commonplace. Direct contact with the rotary blade most often results in damage to the fingers, hand, toes, or feet. However, practically no mention has been made of a more sinister injury which has been encountered since the advent of the rotary power lawnmower. This type of injury is caused by some object being hurled through the air by the rotating blade of the mower. Examination of a rotary lawnmower in action discloses that there is usually a certain amount of debris thrown from under the cowling which houses the blade of the mower. Unevenness of ground or inadequate protection by this shield allows debris thrown by the blade to travel freely through considerable distances. Objects such as glass, steel, wire, stones, or aluminum lying on a lawn can be accelerated rapidly to high speeds, making them similar to war missiles. The force applied to these flung objects must be great judging from the injuries received. In most instances the victims of these injuries have been bystanders who were not operating the lawnmower. This particular missile type of injury is peculiar to the rotary type lawnmower and is not characteristic of the conventional power lawnmower.

—GEORGE R. MILLER, M.D.  
*Southern Medical Journal*  
 pp 982-983 Aug. 1957

## CASE REPORTS

### Dermatomyositis Associated With Pregnancy

FRANKLIN S GLICKMAN *Captain USAF (MC)*

**T**HE purpose of this article is to call attention to the difficult problem of differential diagnosis of the collagen diseases by presenting a patient with dermatomyositis, and to discuss the effects of the association of pregnancy with this disease

#### CASE REPORT

A 27 year old Caucasian woman was first seen on 6 February 1956. At that time she had a pruritic diffusely erythematous facial lesion with butterfly distribution of two months duration. There was no photosensitivity and she was otherwise asymptomatic. Differential diagnosis included seborrheic dermatitis, acne rosacea, and lupus erythematosus (LE). One LE preparation was negative. She was treated with lotio alba.

#### First Hospitalization

On 28 March the patient was hospitalized because of right costo-vertebral angle and right upper quadrant tenderness. She had an upper respiratory infection one week prior to admission and experienced frequency without dysuria or hematuria. Her skin eruption persisted.

*Physical examination* Vital signs were normal. The rash was unchanged. Tenderness was as described. The remainder of the examination was unremarkable.

*Laboratory examination* Red blood cell count was 3.9 million per  $\mu$ l, hemoglobin was 12 grams per 100 ml, and white cell count was 6,000 per  $\mu$ l with a normal differential. Sedimentation rate was 22 mm/hour (corrected). Urinalysis was normal except for a few red and white blood cells on several occasions. Prothrombin time was normal. Bromsulphalein retention (BSP) was less than 5 per cent. Heterophil agglutination was negative. Total protein was 6.9 grams per 100 ml with an albumin of 4.4 grams per 100 ml. Bilirubin was less than 1.0 mg per 100 ml. Cephalin flocculation test was negative. Six LE preparations were negative. Roentgenograms of chest and abdomen were normal. An intravenous pyelogram was negative.

*Hospital course* The patient was treated with Gantrisin (brand of sulfisoxazole) for her urinary complaints and Selsun (brand of selenium sulfide) shampoos for seborrheic scalp changes. An internal medicine consultant advised a high suspicion for collagen disease. She was discharged symptomatically improved after two weeks.

#### Second Hospital Visit

Because of a 15 pound weight loss over the preceding four months the patient was rehospitalized on 10 May. Right upper quadrant tenderness had recurred immediately following her hospital discharge but she had remained afebrile.

*Physical examination* Vital signs were normal. Fine scaling of the erythematous facial rash was noted; there was no atrophy. Right-sided costovertebral angle and upper abdominal tenderness were present. A posterior wall fibroid tumor of the uterus was palpated. Physical examination was otherwise normal.

*Laboratory examination* A complete blood count was unchanged. Sedimentation rate was 32 mm/hour (corrected). Urinalysis was normal. Liver preparations: 20 LE preparations. Liver function studies revealed the following: BSP 17.5 per cent retention; bilirubin 1.5 mg per 100 ml with a direct fraction of 0.7 mg per 100 ml; cephalin flocculation 2 plus in 24 hours and 3 plus in 48 hours; thymol turbidity 4 units; total protein 7.6 grams per 100 ml with 4.4 grams albumin per 100 ml. A trichinella skin test was positive. An electrocardiogram (ECG) was normal. Serology was negative. Roentgenograms of gallbladder, colon, stomach, and small bowel were normal except for a suggestion of hepatomegaly.

*Hospital course* A gynecological consultant concurred in the diagnosis of uterine fibroid tumor and advised no therapy. Right upper quadrant pain persisted and on the tenth hospital day the muscles of both upper arms became painful and tender. An internal medicine consultant advised biopsies of liver, skin, and deltoid muscle.

A repeat blood count revealed 10 per cent eosinophils. Repeat liver chemistry showed a normal BSP and a cephalin flocculation of 1 plus in 24 and 48 hours; other values were unchanged.

Because of the suspicion of collagen disease a trial of Meticorten (brand of prednisone) was begun. On 40 mg per day there was symptomatic improvement in four days.

The liver biopsy was normal; the skin biopsy showed chronic dermatitis but no evidence of collagen disease. The muscle biopsy was interpreted as acute myositis with severe necrosis, consistent with dermatomyositis. The Armed Forces Institute of Pathology concurred in these interpretations (fig. 1).



Figure 1 Photomicrograph of a skin biopsy from the thigh of a patient with dermatomyositis. The epidermis is relatively normal, but the dermis shows a dense infiltrate of inflammatory cells.

A recurrence of muscle pain required an elevation of the dose of Meticorten to 50 mg per day and on this therapy there was progressive improvement. The deltoids, biceps and triceps were noted to be soft with some limitation of movement. Transient tenderness of both gas trocnemius muscles occurred. The 24 hour urinary creatinine was 12 grams and creatine was 0.4 gram (elevated).

The patient was discharged improved on 8 May.

#### Third Hospital Admission

One week later while on 50 mg Meticorten severe muscle pain recurred in all extremities. The patient was rehospitalized the Meticorten was raised to 60 mg and testosterone 25 mg twice a week was added. She improved rapidly was discharged in one week and has not again been hospitalized for her dermatomyositis inasmuch as her symptoms have been maintained under control except for minor flare ups especially noted after minor infections.

The testosterone was discontinued about one month after it was started because symptoms had subsided and the patient had developed a severe case of acne vulgaris. The dose of the Meticorten was gradually decreased by about 5 mg per week. An attempt was made to discontinue it but symptoms recurred and a maintenance dosage of 25 mg per day was finally found to be the lowest amount that would keep her symptom free.

In addition to the Meticorten maintenance therapy included KCl in doses up to 4 grams per day a low salt diet and 25 units of ACTH intramuscularly every other week. Biweekly blood pressure determinations, weight measurements and urinalyses and monthly fasting blood sugar determinations were made. A physical examination was done weekly.

The patient became pregnant in August. Toward the end of the first trimester she developed pyelitis. *Escherichia coli* was cultured from the urine. She was treated with Gantrisin and symptoms subsided. There was no recurrence.

The frequency of minor flare ups of symptoms became gradually less during the course of the pregnancy and it was found that the maintenance dose of the Meticorten could be lowered to 20 mg per day with no untoward reaction.

This was the patient's second pregnancy. She had had no abortions. The first pregnancy had resulted in a normal spontaneous full term delivery. The child was living and well and about 3 years of age.

Obstetrical examination was normal and revealed an adequate pelvis. During the course of the pregnancy the patient was treated as any other prenatal patient except that routine prenatal checks were made every week in conjunction with her medical examination. There were

no complications until the early part of May 1957 about two weeks prior to her estimated date of confinement when she presented with rather copious vaginal bleeding and irregular weak uterine contractions

#### Fourth Hospitalization

On admission the hemoglobin was found to be 7 grams per 100 ml. By the time the consultant in obstetrics arrived the contractions had ceased but the bleeding continued. The cervix was thick soft and dilated about 2 cm. Blood was issuing from the os in moderate amounts. The fetal head was not felt to be engaged. There was no tactile evidence for the existence of a placenta previa. The fetal heart rate was 150 and regular.

Within an hour the bleeding stopped. There were no contractions. The fetal heart tones remained good. The patient's hemoglobin rose to 11 grams per 100 ml following transfusion with two pints of blood. She was observed on the obstetrical ward for several days. There was no further bleeding and she was discharged after four days.

#### Fifth Hospitalization

The patient was again admitted to the obstetrical ward during the first week in June because of moderate contractions every five minutes and a rather heavy bloody show. The fetal heart was regular and of normal rate. After a labor of about six hours the patient spontaneously delivered a seven pound infant who appeared normal in all respects. Examination of the placenta revealed a marginal sinus rupture.

The patient was discharged on the fourth post partum day. Post partum course had been normal. The baby did well on a routine regimen.

Following delivery the patient's Meticorten was raised to 30 mg daily and then gradually reduced in accordance with the scheme mentioned previously. This was done to obviate a possible recurrence of symptoms of the dermatomyositis in the post partum period because of hormonal change.

### DISCUSSION

Dermatomyositis is an acute, subacute or chronic disease that involves the skin, subcutaneous tissue and skeletal muscle.<sup>1</sup> It is of unknown etiology, and is grouped with the collagen diseases.

Clinically, the major findings are tenderness and pain over skeletal muscle particularly of the extremities and a non-specific dermatitis that has certain typical characteristics. Other findings are those which may be found in the other systemic collagen diseases. Creatinuria is a constant finding, and there is a high incidence of eosinophilia.

The onset is commonly noted to follow an upper respiratory infection. The disease may be accompanied by a low grade fever



There is no sex predisposition. The victims tend to be children or young adults. The presenting symptom may be myositis, dermatitis, or any of the systemic manifestations of collagen disease. It has been noted that about 25 per cent of patients with dermatomyositis develop or have neoplastic disease. The relationship is not understood.

The mortality rate in acute dermatomyositis is about 50 per cent. The majority of the remaining patients go on to follow a chronic recurrent course that may go on for years and eventually terminates in death. A small percentage recover from the acute episode and never have a recurrence.

Lupus erythematosus, scleroderma, dermatomyositis, and periarteritis nodosa constitute the collagen diseases. These four entities were first grouped together by Banks in 1941. There is little doubt that the collagen diseases belong together. The question is whether they are really separate entities or part of a single clinicopathologic continuum. There is a good deal of evidence to support the latter view. Talbott states that dermatomyositis may be indistinguishable from acute lupus erythematosus clinically and indistinguishable from scleroderma pathologically. Scleroderma proven pathologically has been reported with positive LE preparations. Sclerodermatomyositis is being recognized as an entity.

In discussing the differential diagnosis of these diseases the above facts should be kept in mind. The "typical" findings in each of these conditions may not be the usual and a confusing mixture may present itself.

On the skin in lupus discoid variety one sees a classic triad consisting of telangiectasia, atrophy, and follicular plugging. In the acute form this classic triad usually does not have time to appear and one sees diffuse erythema with fine adherent scaling, especially in the so called butterfly area. In scleroderma the skin is thin and bound down, as well as atrophic. Pigmentary changes occur in all the collagen diseases. This is secondary to epidermal injury.

The eruption in dermatomyositis classically starts with erythema and edema of the face, particularly in the butterfly area and about the eyes. There may or may not be atrophy. In a series of 25 cases Sheard reported rash on the face or swollen eyelids as the presenting symptom in 32 per cent of the cases. If, however, a patient is seen with odd multiple eruptions or generalized eruption that remind one of collagen disease but are not really typical of anything, and especially if the patient is complaining of muscular weakness or tenderness, then dermatomyositis should be considered.

The clinical manifestations in collagen disease include dermatitis involvement of serous and synovial membranes (polyserositis and polyarthritides), evidence of vascular changes (kidney, retina, nodules), fever, and moderate anemia. The presence of these manifestations should make one think of collagen disease.

From the laboratory standpoint, the sedimentation rate may be elevated and there may be leukopenia. The A/G ratio may be reversed. Lupus is frequently accompanied by a thrombopenia and a false positive serology. Subcutaneous nodules along the course of a blood vessel occur in periarteritis, in this condition the trichinella skin test frequently is positive. Specific findings in dermatomyositis have already been discussed.

Histologically, acute lupus is distinctive, with epidermal atrophy, liquefaction necrosis of the basal layer, and fibrinoid degeneration of the corium. In periarteritis one sees an obliterating panarteritis. In scleroderma the typical findings are thinning and atrophy of the epidermis with obliteration of the appendicular structures and rete ridges, and massive homogenization of the collagen in the corium. In dermatomyositis, one usually finds a necrotizing myositis and findings consistent with chronic dermatitis. Occasionally findings closely resemble scleroderma.

### Therapy

Until the advent of steroid therapy treatment of the collagen diseases was entirely unsatisfactory. Cortisone, in the skin and subcutaneous tissues, acts primarily as an anti-inflammatory agent. It delays the normal inflammatory response even if a stimulus is present. The exact site of action is still controversial but it seems certain that the drug directly affects the vascular bed and at the same time slows or prevents fibroblastic activity. This would explain the effectiveness of the drug in collagen disease.

In treating any disease with parenteral steroids the most effective regimen consists of starting with high doses (60-100 mg daily of Meticorten or the equivalent in cortisone, hydrocortisone, or ACTH) and then gradually decreasing the dosage to maintenance levels that are arrived at by trial and error. If the initial dosage is too low the patient's disease may escape control and increasing dosages may be of no avail.

Complications of steroid therapy occur and precautions must be taken. Frequent physical examinations should be made. ACT to prevent hypokalemia and a low salt diet to prevent hypertension are essential. Periodic checks for hypertension, weight gain, glycosuria and hyperglycemia should be done. Fortified

electrocardiograms are indicated. Any evidence of concurrent infection should be vigorously handled with high doses of antibiotics to prevent dissemination. Personality changes should be watched for. The patient should be told to inform the doctor immediately of any tarry stools or abdominal pain.

The results of steroid therapy in collagen disease have not been consistently good. This is true in dermatomyositis. McElligott stated that the steroids are more effective in the acute cases and usually fail to improve the chronic cases. He went on to say that the drugs should not be withheld from these people however, because there have been some reported successes. Lamb and Jones believed that the steroids should rarely be used in dermatomyositis, claiming that they are only effective in about 20 per cent of cases. They preferred testosterone as the therapy of choice. The rationale for this is that since dermatomyositis is a necrotizing myositis primarily, the anabolic effects of testosterone should aid considerably in preventing muscular destruction.

#### Dermatomyositis and Pregnancy

There is no reference to dermatomyositis with accompanying pregnancy in the recent literature. Andrews describes a case of sclerodermatomyositis that started after childbirth. There have been reports in the literature of scleroderma and lupus with pregnancy. The consensus is that the disease either improves or is not affected by the pregnancy. This is ascribed to increased output in pregnancy of steroids and steroid-like hormones. This point is still controversial. It appears that there is an increased rate of abortion in patients with collagen disease.

Our patient was followed for almost two years. It was our impression that a clinical remission took place during the pregnancy. Objectively, we found that we could lower the dose of the steroid. In coming to this conclusion it must be borne in mind that spontaneous remissions in dermatomyositis do occur. We were concerned with the possible effects of the drug on the infant. There were none. The child was perfectly normal. We also were concerned with the possibility of a flare of the dermatomyositis during the post partum period. We therefore increased the dose of Meticorten immediately following delivery and then gradually returned to a maintenance dose. No flare up of symptoms was noted.

#### SUMMARY

A case of dermatomyositis associated with pregnancy has been presented with emphasis on the differential diagnosis of collagen disease and the effects of pregnancy on collagen disease.

This patient was treated with Meticorten, ACTH, and test osterone. She delivered a normal, full term infant. There appeared to have been a remission during the pregnancy. There was no post-partum flare.

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### CORONARY ARTERY DISEASE AS REPORTED CAUSE OF DEATH

"The publicity given to the rise in coronary artery disease has of itself led to greater awareness of the disease. As a result, an increasing number of deaths are being reported as due to coronary disease by coroners and medical examiners where the deceased had not received medical attention or the cause of death was not known. In one area of the country more than 35 per cent of the deaths reported as coronary disease were certified by the medical examiner's office. In New York City in December 1956 some 15 percent of the deaths from arteriosclerotic heart disease and 44 percent of the deaths attributed to coronary artery disease were medical examiner's cases. Only a very small proportion (4 percent and 9 percent respectively) of these diagnoses were verified by autopsy.

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Metropolitan Life Insurance Co  
p 3 Feb 1957

# Hepatic Cirrhosis Mistaken for Lupus Erythematosus in a Young Girl

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**I**N 1956 Bearn, Kunkel, and Slater<sup>1</sup> reported 26 cases of severe hepatic cirrhosis of undetermined cause in young women. Ethanol, nutritional deficiency, and viral hepatitis were excluded as etiologic agents in their series. Our case falls in the same category and is thought to be important in that there was an apparent involvement of multiple systems. Because of this apparent involvement, a mistaken diagnosis of lupus erythematosus was made originally.

## CASE REPORT

The patient was a 14-year-old Caucasian girl who was first hospitalized on 4 August 1956 because of bilateral ankle edema. During the previous year she had had frequent epistaxes, a nonproductive cough, and fatigue, all of which were aggravated by exertion. Three months before her admission to the hospital she was seen by a physician for persistent orbital headache and suffusion of the conjunctiva. No significant abnormalities were found, and these complaints subsided spontaneously. Two months before admission she had had an unusually severe nosebleed that lasted two days. This was followed by a temperature of 102 F, abdominal pain, and diarrhea lasting 24 hours. At this time there was pain in the muscles of both legs which interfered with ordinary activity, and at times was associated with localized edema.

Periorbital edema was present each morning on arising and persisted for two or three hours. The edema continued to recur until just before the patient's admittance to this hospital. One month before this admission she noticed a marked increase in fatigue and swelling of one leg that persisted for two days. One week before hospitalization she complained of dizziness and diarrhea and had a temperature of 102.2 F. She was treated for gastroenteritis, and the symptoms sub-

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sided after one day. On 3 August she had bilateral ankle edema and was hospitalized the following day.

As an infant the patient had had pneumonia and bronchitis as well as the common acute exanthemas of childhood. She denied having had scarlet fever or rheumatic fever either by name or by symptoms and there had been no jaundice beyond the neonatal period. The menarche had occurred six months prior to her admission and was followed by amenorrhea.

The patient was well nourished, well developed and did not appear ill. Her height was 67 inches, weight 120 pounds, temperature 98°F, pulse rate 88 per min, respiration 20 and blood pressure 128/80 mm Hg. She had no rash but there was 1 plus pitting edema of her ankles bilaterally. Her head, eyes and ears were normal. Her nose showed only increased vascularity of the mucous membrane. The remainder of the physical examination was normal except for the abdomen where a firm, nontender mass was noted in the left upper quadrant extending 5 cm below the costal margin. The mass was thought to be the spleen and on intravenous pyelography it could be seen displacing the left kidney downward.

Initial urinalysis revealed a specific gravity of 1.030 and 2 plus proteinuria. Numerous erythrocytes and granular casts were noted in each high power field. Subsequent specimens of urine were unchanged except that erythrocytes and casts were noted only on one other occasion. Blood studies showed a leukocyte count of 4,000 per  $\mu$ l with 58 per cent neutrophils and 42 per cent lymphocytes. Hemoglobin was 13 grams per 100 ml, hematocrit 35 ml per 100 ml and the sedimentation rate 19 mm per hour (Wintrobe). Prothrombin, bleeding, coagulation and clot retraction times were normal. Serologic tests for syphilis were consistently negative. Blood urea nitrogen was 15 mg per 100 ml. Total serum cholesterol was 126 mg per 100 ml with ester fraction of 31 per cent. Total serum protein was 5.0 (albumin 2.14, alpha globulin 0.61 and beta globulin 2.25) grams per 100 ml. C-reactive protein and antistreptolysin titers were negative. No lupus erythematosus (LE) cells or allied phenomena were found on repeated examination. The thymol turbidity was 12.8 units, cephalin cholesterol flocculation 4 plus in 24 hours and there was 31 per cent retention of Bromsulphalein 45 minutes after intravenous injection of 5 mg per kg of body weight.

During her initial hospitalization the patient had had several minor episodes of epistaxis which were easily controlled. Aside from this she had no complaints and after 33 days in the hospital she was discharged with a presumptive clinical diagnosis of a diffuse collagen disease. Three days later she was readmitted because of further epistaxis, marked malaise, fatigue and pain and tenderness in the left calf.

On this admission the leukocyte count was 3,300 per  $\mu$ l with a differential count of 47 per cent neutrophils, 12 per cent eosinophils

1 per cent basophils 36 per cent lymphocytes and 4 per cent monocytes A few target cells and spherocytes were noted and the platelets appeared to be slightly decreased A serologic test for syphilis was negative Total serum bilirubin was 1.32 mg per 100 ml with a direct bilirubin of 0.24 mg per 100 ml The Bromsulphalein test showed 40 per cent retention at the end of 45 minutes Thymol turbidity was 15.7 units and cephalin cholesterol flocculation was 4 plus in 48 hours Prothrombin time was normal on entry but fell to 63 per cent activity while the patient was in the hospital LE preparations were consistently negative

In spite of abnormal findings in the liver function tests it still was believed that the patient had lupus erythematosus or less likely polyarteritis nodosa because of symptoms and laboratory findings suggesting multiple system involvement and the lack of physical evidence of hepatic disease A muscle biopsy from a tender site in the left calf was normal Bone marrow aspiration showed a normal cellular marrow

Needle biopsy of the liver was attempted twice without success On the first attempt sedation was accomplished with 100 m of pentobarbital sodium and 50 mg of meperidine hydrochloride Following this medication the patient was drowsy and somewhat confused for two days which apparently was due to the medication as no untoward effect was noted from the biopsy itself

During the second hospital course intermittent pain in the left upper quadrant became a serious problem Two milligram doses of dihydromorphine hydrochloride were required for relief of pain This drug produced no untoward effect Examination disclosed only an enlarged tender spleen Repeat leukocyte counts were unchanged showing a slight leukopenia with a normal differential count During her third hospital week the patient had a temperature of 102 F with nausea vomiting and constant left upper quadrant pain but no significant changes were noted either on physical or laboratory examination She was treated symptomatically and after three days the symptoms began to clear After one week only the inconstant pain in the left upper quadrant remained After 32 days the patient was again discharged to her home symptomatically improved and with a diagnosis of probable lupus erythematosus

After leaving the hospital the patient had a low grade fever marked weakness and more frequent epistaxis She was admitted on 26 October for the third time only three weeks after discharge Physical examination revealed no new findings The hemogram was essentially unchanged the platelets numbered 152 000 per  $\mu$ l Urinalysis showed 2 plus albumin 2 to 4 granular casts with an occasional erythrocyte or leukocyte per high power field Serum alkaline phosphatase was 10.8 Bodanaky units total serum cholesterol was 232 mg per 100 ml with ester fraction of 68 per cent and on 27 October the total serum

protein was 5.43 (albumin 3.28) grams per 100 ml. Repeat LE preparations were negative. Prothrombin ranged from 50 to 70 per cent activity and was not affected by vitamin K<sub>1</sub> oxide. Maximal postoperative serum bilirubin was 14.0 mg per 100 ml with a direct bilirubin of 7.0 mg per 100 ml. Thymol turbidity was 16.7 units and cephalin cholesterol flocculation was 4 plus in 48 hours. Bromsulphalein retention was 43.8 per cent at 45 minutes.

The original diagnosis of a diffuse collagen disease now seemed unlikely in view of the persistently negative LE preparations and the negative muscle biopsy. The timely article by Bearn, Kunkel and Slater<sup>1</sup> on hepatic cirrhosis of obscure cause revealed a striking similarity between this patient and those they described. Roentgenographic examination of the upper gastrointestinal tract failed to show any evidence of esophageal varices. The only abnormality noted was a pressure defect of the stomach as a result of the large spleen. The liver shadow appeared small.

On 13 November an exploratory laparotomy was done to confirm the diagnosis of hepatic cirrhosis and to perform a portacaval shunt if warranted. When the liver was visualized its total size was only about one third to one half the normal size. It was hard and the surface was studded with small nodules of regenerating liver tissue. The spleen was smooth and firm and was two to three times the normal size. The appearance of the mesenteric veins did not suggest an increased portal pressure. By direct measurement, however, the pressure in the portal vein was found to be 250 mm of water. The appearance of the liver indicated far advanced cirrhosis with a very poor prognosis. It therefore was decided that a portacaval shunt was not indicated but a liver biopsy was performed.

The specimen showed the architectural pattern distorted by heavy bands of connective tissue which surrounded lobules to form nodules from 2 to 3 mm in diameter. Many of the lobules showed intact central veins with preservation of the surrounding liver cells. The separating connective tissue septums contained increased numbers of rudimentary bile ducts and a diffuse infiltration with lymphocytes, neutrophils and a few eosinophils. The presence of numerous portal canals which were either within normal limits or only slightly altered and which did not enter into the formation of pseudolobules met the criteria for the diagnosis of postnecrotic cirrhosis (fig. 1).

The patient's immediate postoperative course was uneventful except for a gradual increase in the serum bilirubin. Three weeks after surgical intervention there was a sudden sharp increase in the serum bilirubin associated with the appearance of ascites and accompanied by anorexia and marked weakness. The patient was treated with a low salt diet and chlortetracycline hydrochloride (aureomycin) with only minimal improvement.

Because of the critical nature of her disease it was her parents' desire that the patient return to the United States. She therefore was



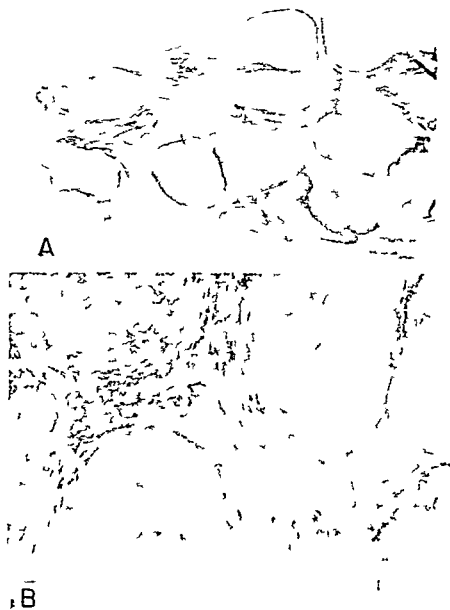


Fig 1. Low power photomicrograph of liver tissue (A,  $\times 14$ ). High power photomicrograph of liver tissue (B,  $\times 50$ ).

transferred to an Army hospital in the United States where gradual improvement ensued. Her jaundice slowly subsided and the ascites drained spontaneously through the abdominal incision. Laboratory findings were essentially unchanged except for a total serum protein of only 4.3 grams per 100 ml with a reversal of the albumin globulin

ratio Treatment consisted of a low salt adequate protein diet with multiple vitamins and mercurial diuretics There was gradual clearing of the ascites and closure of the wound

During convalescence thrombophlebitis occurred in both legs This was managed with heparin sodium without untoward incident After two and one half months the patient improved sufficiently to be discharged to her home Since then she has been able to carry on moderate activity and there has been no recurrence of jaundice Minimal ascites and peripheral edema persisted for about seven months postoperatively and then subsided Mild infrequent pain in the left upper quadrant of her abdomen has remained Amenorrhea also has persisted There were no spider nevi nor any palmar erythema at any time during her illness

### DISCUSSION

In patients with juvenile cirrhosis, the clinical picture at the onset of symptoms may be confusing and difficult to diagnose In the report of Bearn Kunkel and Slater obesity amenorrhea fatigue, and epistaxis were all listed as presenting complaints The patient in this report noted exertional fatigue with epistaxis and amenorrhea as her earliest symptoms On examination however, only splenomegaly suggested the possibility of liver disease until icterus appeared during her third admission

When first seen symptoms in these patients may suggest involvement of other systems Amenorrhea or delayed menstruation for instance may suggest a primary local pathologic condition or an endocrine disturbance particularly if associated with obesity In the 26 patients with cirrhosis reported by Bearn and associates all but two had hepatosplenomegaly and these two had hepatomegaly

In reviewing the literature on systemic lupus erythematosus Harvey and co-workers<sup>2</sup> noted hepatomegaly in 35 per cent of 105 patients and splenomegaly in 15 per cent The liver usually extended 2 to 3 cm below the costal margin Bromsulphalein retention tests were performed on 16 of these patients and an abnormal retention was noted in 6 Three of these had either cirrhosis of the liver or viral hepatitis Prothrombin times were determined in 38 patients and in 7 showed a moderate reduction to about 50 per cent of normal In 6 patients there was a marked reduction to less than 30 per cent activity Vitamin K had no effect on restoration of the prothrombin time to normal Cephalin flocculation and thymol turbidity determinations were made in 82 cases by Harvey and co-workers They were positive in 67, probably because of altered protein relationships

The splenomegaly in our patient together with her very poor hepatic function tests should have suggested the correct diagnosis on her first admission However the absence of hepatomegaly and of any antecedent history of jaundice or symptoms

usually ascribed to cirrhosis led us to a misdiagnosis. The myalgia, epistaxis, leukopenia and hematuria noted on at least two occasions and the repeated albuminuria caused us to make the diagnosis of systemic lupus erythematosus. As the patient's course progressed and after rereading the paper of Bearn and associates it became increasingly apparent that she had liver disease and not systemic lupus erythematosus as was thought originally.

### SUMMARY

Postnecrotic cirrhosis may initially resemble systemic lupus erythematosus as illustrated by a case report of a 14 year old girl. In young women the prominent features of this disease are fatigue or malaise aggravated by effort, amenorrhea or delayed menarche, arthralgia and jaundice. Hepatosplenomegaly or either hepatomegaly or splenomegaly alone may be the only significant physical abnormality encountered in the absence of jaundice.

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### SPECIFICITY IN THERAPY OF THE FUTURE

The therapy of the future will be increasingly selective and more and more will assume the sharpness of the surgeon's knife as it invades the tissue to be affected. This selectivity may in some instances lessen the threat of side reactions but in others may increase the dangers. Thus it doesn't seem practical at this time to dream of the broadly acting drug that will attack many diseases without any harmful possibilities. Antibiotics and the sulfonamides have a wide sweep in their effectiveness but they probably will not be representative of most drugs of the future. While it is possible to attach many criteria with one agent, other health problems will require the specificity of many of the drugs now under development. While there seem to be many magic bullets today in the field of chemotherapy they cannot be expected singly to win the war against disease any more than one rifle would have taken Anzio beach in World War II.

—AUSTIN SMITH M D  
in *Journal of Natural Medicinal Association*  
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# Parkinsonism in an Oriental Treated by Chemopallidectomy

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**P**ARKINSONISM is a disturbance of motor function, characterized chiefly by slowing and weakening of voluntary movement, muscular rigidity, and tremor. The syndrome may be produced by any of several pathologic processes. It usually is ascribed to lesions involving the corpus striatum, globus pallidus or substantia nigra. The condition usually develops insidiously and progressively, but frequently is marked by partial remissions, plateaus, and exacerbations of varying duration. It may be unilateral or bilateral.

During the past 20 years, various surgical procedures<sup>1-5</sup> have been carried out to relieve the spasticity and tremor, but their success has been proportional to the sacrifice of motor power. Other techniques<sup>6</sup> were aimed at the basal ganglia; however, high operative mortality precluded their general use. Recently, stereotactic apparatus was used by Spiegel, Wycis, and Thur<sup>7</sup> and Narabayashi and Okuma<sup>8</sup> for approach to the basal ganglia, while Penlon and Thiebaut<sup>9</sup> devised methods of coagulating the ansa lenticularis and globus pallidus without the use of a stereotactic machine.

During the past several years Cooper<sup>10-12</sup> and co-workers devised techniques aimed at the destruction of the mesial globus pallidus and its afferent connections with other basal ganglia and motor areas of the brain. The first of these was anterior choroidal artery occlusion which aimed at infarction of the mesial globus pallidus by interfering with its blood supply. The second was chemopallidectomy,<sup>13</sup> which aimed at the destruction of the mesial globus pallidus by injection of absolute alcohol into this structure. It is the latter of these procedures that we have used in the case to be presented.

## METHOD

The technic of chemopallidectomy described by Cooper<sup>10</sup> and Cooper and Poloukhine<sup>11</sup> consists of placing a small polyethylene

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# Congestive Heart Failure of Undetermined Cause

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**C**ONGESTIVE heart failure usually is secondary to definite cardiovascular abnormalities and ordinarily the origin of the syndrome can be fairly well determined. In young adults it is a relatively rare phenomenon except in association with rheumatic or congenital heart disease or as a complication during the course of acute glomerulonephritis and idiopathic congestive heart failure is almost unknown. Rosenbaum, Nadas, and Neuhauser reported several cases of what they considered to be idiopathic myocarditis in infants and children but none in an adult.

## CASE REPORT

A 29 year old soldier was admitted to this hospital on 4 April 1957 with the chief complaint of swelling of the face and legs of two weeks duration. The past and family histories were noncontributory. The patient stated that he had felt perfectly well until about two weeks prior to admission when he noted the onset of painless swelling of the face. This did not trouble him at the time and he did not seek medical attention until 26 March 1957 when at his wife's insistence he reported to sick call and was diagnosed as having angioneurotic edema of the face.

It was noted by the examining physician that the patient had had two similar episodes in the past two or three years and each time had been cutting grass prior to the onset of his difficulty. Because of this history skin sensitivity tests were accomplished by the scratch method but were negative. The patient was given 50 mg of Benadryl Hydrochloride (brand of diphenhydramine hydrochloride) four times daily. This did not alter his clinical status. He returned to sick call on 28 March at which time he complained of some swelling of the abdomen. The examining physician stated that there was some edema of the upper abdomen and prescribed 24 mg of ephedrine sulfate four times daily in addition to the Benadryl which the patient was already taking.

Shortly thereafter the patient noted that his legs were beginning to increase in size. On 29 March he again returned to sick call because

of headaches. At that time he had typical physical findings of acute sinusitis and roentgenograms of the paranasal sinuses confirmed this diagnosis. He was treated by the application of heat to the forehead and sodium salicylate was now added to the therapeutic regimen. The patient stated that at this time he felt that his abdomen seemed to improve but his ankle edema increased and he began to have shortness of breath on exertion. He noted that lying down on his stomach would markedly increase the shortness of breath and found it was necessary to use two pillows rather than the usual one in order to avoid dyspnea while lying down. There had been absolutely no past history of cardiac or renal disease.

The patient returned to sick call on 4 April. At that time it was noted that his blood pressure was 180/105 mm Hg. There were rales at both lung bases hence the patient was admitted to the hospital for further evaluation and therapy.

Physical examination on admission revealed a well developed and well nourished white man who was in no distress. His temperature was 98.2°F, pulse 92, blood pressure 170/100 mm Hg, height 6 feet 1 inch, weight 160 pounds. There were numerous medium moist rales at both lung bases. The heart size was normal to percussion and the rhythm was normal. The second aortic sound was somewhat loud and there was a grade I systolic murmur heard generally over the precordium. There were no diastolic murmurs. Examination of the abdomen showed the liver to be palpable two fingersbreadth below the right costal margin. It was slightly tender and smooth. No other masses were palpated. There was 2 plus pitting edema of both lower legs. The remainder of the physical examination was either negative or within normal limits.

A hemogram showed a white blood cell count of 11,400 with 73 per cent neutrophils, 2 per cent eosinophils, and 25 per cent lymphocytes. The hemoglobin was 12.5 grams per 100 ml and the sedimentation rate was 48 mm per hour. The original urinalysis revealed a few white blood cells without other abnormal findings. The serologic test for syphilis was negative. Blood chemistry studies on 5 April showed the following values: nonprotein nitrogen 21.6 mg per 100 ml, blood urea nitrogen 10.2 mg per 100 ml, serum chlorides 108 mEq/l, serum sodium 145 mEq/l, cholesterol 236 mg per 100 ml with 170 mg per 100 ml as esters. The total serum protein was 5.8 grams per 100 ml (albumin 2.9 grams and globulin 2.9 grams). The initial roentgenogram of the chest (fig. 1) demonstrated the heart to be the upper limit of normal size with bilateral basilar pulmonary congestion. There was a small amount of pleural fluid in the costophrenic angles bilaterally. It was the roentgenologist's opinion that these findings were typical of congestive heart failure. Fluoroscopy revealed only that the size of the heart was at the upper limit. The electrocardiogram was normal.

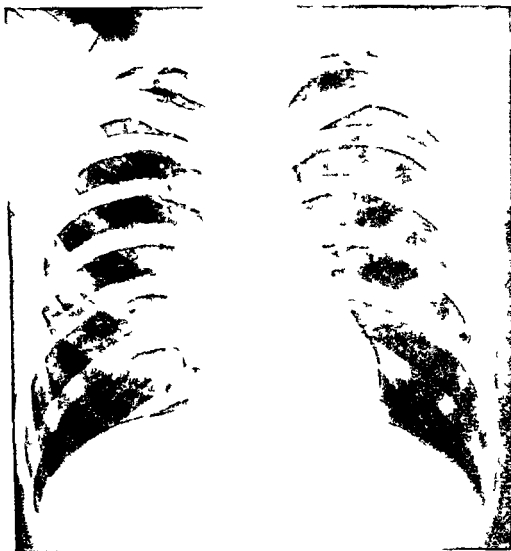
The patient was kept in bed and was given a low sodium diet. No other specific medications were administered. On this program he



Figure 1 Roentgenogram of chest taken 4 April 1957. Note fluid in pleural space and blurring of lung fields.

improved dramatically. His weight on admission was 160 pounds and within five days he lost 18 pounds. Venous pressure on 5 April was 160 millimeters of saline. The circulation time using Decholin (brand of dehydrocholic acid) was 14 seconds. It was thought that in this man who was of slight stature this time was slightly prolonged. Daily urinalyses revealed no specific abnormalities although on 5 April there was a 1 plus albumin. After this specimen the urine examinations were entirely normal. An Addison count was normal. A 24 hour urine sample on 8 April revealed a total protein content of 0.01 gram per liter and repeat blood urea nitrogen and nonprotein nitrogen were normal.

On 9 April the patient was allowed to be ambulatory about the ward and was given a regular diet. The abnormal pulmonary findings cleared rapidly. The fluid in the costophrenic angles and systolic murmur heard disappeared. A roentgenogram of the chest on 10 April (fig. 2)



*Figure 2 Roentgenogram of chest on 10 April 1957 Note decrease in heart size and disappearance of pulmonary edema and pleural fluid*

revealed decrease in the size of the heart from an original transverse diameter of 14 cm to 11 cm. Serial electrocardiograms were entirely normal.

On 18 April the patient was allowed two weeks of convalescent leave from which he returned on 6 May having remained entirely asymptomatic. Physical examination upon his return to the hospital revealed no abnormalities. The heart size was normal and there were no murmurs. Blood pressure was 118/76 mm Hg.

Electrolyte studies on 6 May revealed the serum sodium to be 131 mEq/l, potassium 4.4 mEq/l, and chlorides 98 mEq/l. Total serum protein was 6.8 (albumin 3.5 and globulin 3.3) grams per 100 ml. After the initial two to three days in the hospital the patient seemed to be clinically normal. Renal function studies, urinalysis, blood urea nitrogen, and urine concentration tests were normal at this time. An electrocardiogram and a roentgenogram of the chest were normal.



The patient was discharged to duty on 8 May and was advised to remain on limited duty for three months after which he was returned to full military duty. He was followed as an outpatient and in serial follow up studies it was noted that his blood pressure remained in the vicinity of 115 to 120 over 65 to 70 mm Hg. Auscultation of the heart revealed no abnormality. Electrocardiograms and roentgenograms of the chest remained normal. Basal metabolic rate was +5. The patient is at the present time (November 1957) performing full military duty and remains completely asymptomatic.

### SUMMARY

This patient is presented as representing an unusual case of congestive heart failure of unknown cause. At the time of his admission to the hospital it was assumed from his clinical history that he probably had acute glomerulonephritis as the underlying cause of his difficulty. He had edema and hypertension and an isolated urine specimen had revealed pyuria. However, serial urine studies and blood chemistry studies made this diagnosis untenable. The possibility of pericarditis was considered but this seemed extremely unlikely in view of the normal electrocardiograms, the absence of friction rubs and the presence of normal cardiac fluoroscopy. Hypertension in this patient was extremely short-lived and was present only during the first day of his hospitalization. There was no evidence for allergic vasculitis with myocarditis or for acute bacterial or viral myocarditis. He recovered completely from his episode of congestive heart failure, has no residuals and is performing full active military duty without handicap eight months after his hospitalization. It is most unusual for a 29-year-old healthy white man to develop acute congestive heart failure and yet this is the case in this individual. He recovered quickly with bed rest and a low sodium diet. It is thought that the latter had nothing to do with the patient's recovery; however, Digitalis was not used in the management of this case.

### REFERENCE

1. R. Baum, H. D. N. d. A. S. and N. uha. r. E. B. D. P. mary my ca dia!  
d. l. cy. d. b. ldb. od. A. M. A. Ann. J. Di. Ch. Id. 86: 28-44. J. ly 1953.

### AERO MEDICAL ASSOCIATION MEETING

Geared to the forthcoming age of space travel more than 100 speakers will present the latest research and development achievements in the biologic aspects of flight at the 29th annual meeting of the Aero Medical Association at the Statler Hotel Washington D C 24 25 and 26 March 1958 Captain Ashton Graybiel MC USN director of research at the U S Naval School of Aviation Medicine is president of the society

Sessions on space flight will be held on the afternoons of 24 and 26 March under the chairmanship of Colonel Paul A Campbell USAF (MC) and Doctor Hubertus Strughold respectively The program also includes papers on acceleration oxygen equipment hypoxia and hyperoxia human behavior sensory problems hyper- and hypothermic stress physiology psychology civil aviation medicine and clinical problems

The fourth Louis H Bauer lecture established in 1955 as a tribute to the Association's founder and first president will be presented on 24 March as a part of the opening ceremony of the meeting by Doctor Rodolfo Margaria distinguished professor of physiology and biochemistry at the University of Milan He will present new phases of recent work in acceleration and fatigue

In addition to a full scientific program Captain Graybiel will be host at an international reception for visiting members and guests from other countries at the Officers Mess of the National Naval Medical Center Bethesda Md on the evening of 25 March He will also preside at the traditional banquet of the Association at the Statler Hotel on 26 March when the recipients of the Association's four awards for aeromedical achievement will be announced

Brigadier General M S White USAF (MC) president elect of the Aero Medical Association will be installed as Captain Graybiel's successor The Airline Medical Directors Association and the Civil Aviation Medicine Association will hold concurrent meetings in Washington



*Captain Graybiel*

## A MESSAGE FROM THE A M A

Two resolutions introduced during the 3 to 6 December 1957 meeting of the American Medical Association in Philadelphia are of particular interest to physicians in the military services. One of these concerns service membership in the Association and the other recommends a program to encourage participation of federal service physicians in local medical societies.

Resolution No. 7 was referred to the Reference Committee on Amendments to the Constitution and Bylaws. In view of the complexity of this question which involves changes in the constitution and bylaws of the Association, the Committee recommended that the matter be referred to the Council on Constitution and Bylaws for further study. The recommendation was adopted by the House of Delegates and provides as follows:

Whereas A basic principle of organized medicine in America holds that an applicant's qualifications for membership should be evaluated by his local colleagues and that when he is elected to membership in a county medical society he should then and then only become a member of his state medical association and the American Medical Association and

Whereas Direct Service Membership in the American Medical Association designed to meet certain necessities of career officers in the Armed Forces of the United States has over the years been expanded far beyond that original concept and has reached the point where it now includes most of the physicians employed by the federal government and removes them from any responsibility to their county and state medical organizations thus violating the basic principle referred to above and

Whereas This expansion has come about largely through piecemeal amendment of the Constitution and Bylaws of our Association some sections of which appear to conflict with each other in matters of choice between dues exempt Active Membership and direct Service Membership and

Whereas Conflicts or optional choices between such membership sections of the Constitution and Bylaws have recently been interpreted by the Board of Trustees and the General Officers in favor of further expansion of Service Membership now therefore be it

*Resolved* That the House of Delegates reiterate its adherence to the principle that membership in this Association should originate with membership in a component county medical society and instructs the Council on Constitution and Bylaws to prepare the necessary

F m th C l N al D feo f th Am ca M d cal A Tb  
w d p p d ar t c sa ly h f h D p rtm f D f  
—Editor

amendments to return Service Membership to the original concept of its applicability only to the career officers of the Armed Forces of the United States and be it further

*Resolved* That pending implementation of these amendments the Board of Trustees and the General Officers are instructed to resolve existing conflicts within the Constitution and Bylaws related to this subject matter in favor of dues exempt active membership through component societies and constituent associations rather than in favor of direct Service Membership

Resolution No 29 was referred to the Reference Committee on Medical Military Affairs The reference committee recommended adoption of the resolution with minor changes in its language This was adopted by the House of Delegates As approved, the resolution provides as follows

Whereas There are approximately 10 per cent of the active practicing membership of the A M A in Federal Medical Services increasing annually the relative percentage of these physicians to the total number of practicing physicians and

Whereas These physicians are not dues paying members of the A M A nor may they vote and

Whereas Active participation of these physicians is sorely needed in all county and state medical association and

Whereas In most if not all county medical societies there are relatively few members of the Federal Medical Services participating to any extent in the activities of these local medical societies and

Whereas It is extremely difficult to enlist active participation of these physicians in local medical societies especially if dues however small are charged as long as non paying membership in the A M A is offered and therefore be it

*Resolved* Membership in the American Medical Association of physicians engaged in Federal Medical Services be reconsidered by the Council on Constitution and Bylaws that this council be requested to seek means of increasing active participation of physicians in this classification and in local medical societies and be it further

*Resolved* That the Council on National Defense through its Committee on Military Medical Affairs assist in the accomplishment of this objective and report back to the House of Delegates of the A M A in 1958 and be it further

*Resolved* That the Surgeons General of the Army Navy Air Force and Public Health Service Veterans Administration and other allied branches be requested to participate in this program and that special recognition or credit be granted to physicians in Federal Medical Services who participate actively in local medical societies

## DEATHS

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YATES M Tw ty C pt MC USN f Darli gt S C. t t on d t U S M Corp At St tion M m Fl graduat d n 1935 f om th M d al Colleg f South C ol Ch l to S C. app ted L t ant jun g d th U t d St t N vy 1937 d d 14 D cember 1957 g 48 at the U S. Mar C p A St tion M m Fl f co a y th om-bo

## THE MULTIPLICITY OF CERTAIN UPPER GASTROINTESTINAL LESIONS

Two special features of the diseases of the upper gastrointestinal tract contribute uniquely to the difficulty of clinical diagnosis. Perhaps the source of greatest confusion is the propensity of localized lesions to produce important nearby and far-removed visceral dyskinesias which more than the lesion itself become responsible for symptoms. Thus many of the diseases produce similar complaints.

Second, more than any other organ system, the gastrointestinal tract is peculiarly susceptible to synchronous multiplicity of localized lesions. In some cases, such as Saint's triad (hiatus hernia, gallstones, and diverticulosis of the colon), combinations occur with such regularity that some causal association must be assumed. In others, the associations seem haphazard. The possible specificity of such associations is of considerable practical and theoretical importance, but for the present study, the question was simply one of how frequently the clinician might expect to encounter another nearby lesion in the upper gastrointestinal tract after one has been detected.

To obtain an impression from personal experience, the lesions shown in table 1 were selected, and charts were reviewed until data from the numbers indicated had been collected. The lesions were chosen with several criteria in mind: they are lesions of the gastrointestinal tract proper; they occur in rather close anatomic relationship;

TABLE 1. Lesions occurring in the upper gastrointestinal tract

	N b f	P h								
		h	E ph l	E ph l d ulum	E ph l	H h rn	G l	G d ul	G ar om	D o- d ul
Esoph ul	30	4		6	33	0	33		33	13
Esoph d l	35	46	5		29	23	29		29	12
E ph l	30	6		33			33			
H h rn	250	25	24	32			11	12	08	14
G l	250	32	04	04	04	11		04	04	25
G d ulum	0	30				15	50			70
rc	00	0		10		20	10			70
Duod l	000	0	04	04		36	62	04	07	

to one another they represent benign malignant and mechanical lesions and although the patients in each category were consecutive clinic and ward patients investigated only as the individual clinical situations warranted they necessarily had approximately the same diagnostic studies (upper gastrointestinal roentgenography in all esophagogastrosomy in most and examination at operation or autopsy in many)

The findings shown in the table need little explanation or comment. Obviously when a sick person is found to have two distinct lesions in the organ system which is responsible for the symptoms the chances are good that one of the lesions either has caused no illness being detected merely by a fortuitous examination or has some etiologic relationship to the other lesion. The first explanation seems especially likely for many of the cases of esophageal diverticulum and the second for cases of multiple lesions associated with hiatus hernia. Patients with carcinoma were found least likely to have an associated lesion. Those with duodenal ulcer were surprisingly free of second lesions unlike the situation found in the cases of gastric ulcer. Conversely when some other lesion was present duodenal ulcer was a very common accompanying problem.

EDDY D PALMER Lt Col MC USA  
2d G I H p t l  
APO 180 New York NY

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## World Congress of Gastroenterology To Be Held in Washington D C

The First World Congress of Gastroenterology (Host Organization American Gastroenterological Association) will be held in the United States in Washington D C from 25 to 31 May 1958 at the Sheraton Park Hotel.

Over 200 national and international scientists physicians surgeons roentgenologists and parasitologists will present the most recent clinical and investigative advances in gastroenterology. Those scheduled to appear on the program will include 36 from the United States and over 160 from 43 other countries. Simultaneous interpretation of the papers presented will be in four languages including German Spanish French and English.

For information relative to the World Congress of Gastroenterology attendance accommodations registration program activities et cetera contact Dr H Marvin Pollard Secretary General World Congress of Gastroenterology University Hospital Ann Arbor Mich.

## ARMY NURSE RECEIVES BOVARD AWARD

Captain Lenora B Weirick ANC Letterman Army Hospital, San Francisco California was selected to be the first recipient of the Evangeline P Bovard Award

This award was established in honor of Evangeline P Bovard an Army nurse from 1912 to 1916 and from 1916 to 1917 with an outstanding record of service in various assignments Following her death at Letterman Army Hospital in 1955 her husband Colonel Robert Skelton MC USA Retired set up this commemorative award by creating an endowment trust fund of assets totaling approximately \$25 000 the earnings of which are to be presented annually for the use and benefit of Army nurses assigned to Letterman Army Hospital



Captain Weirick

Standards for the selection of the individual nurses are based principally on the Florence Nightingale Pledge for Nurses

*"I will do all in my power to maintain and elevate the standards of my profession With loyalty will I endeavor to aid the physician in his work and devote myself to the welfare of those committed to my care*

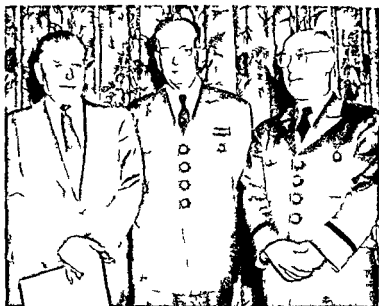
Captain Weirick was selected because of her outstanding qualities in the care of acutely ill patients her invaluable contributions to improve the care of paraplegics and her ability to instruct and train corpsmen that they might become proficient in the care of neurosurgical patients She is a member of the Regular Army and received the Bronze Star for meritorious service in Korea with a Mobile Army Surgical Hospital from 6 April 1951 to 22 April 1952

The Evangeline P Bovard Award consisting of a citation certificate and check was presented to Captain Weirick by Brigadier General Paul S Fancher commanding general of Letterman Army Hospital in a ceremony at the hospital on 14 January 1958



## WALTER REED RESEARCHER RECEIVES PATENT FOR COSMETIC GLOVE

A Letters Patent for an improved prosthetic hand covering that defies detection even on close inspection was presented on 7 January 1958 to the coinventor Carl A. Nielson of the Army Prosthetics Research Laboratory, Walter Reed Army Medical Center, by Major General Leonard D. Heaton, Commanding General of the Center.



From left: Capt. M. Carl A. Nielson, holder of Letters Patent No. 2,811,601; Major General Leonard D. Heaton, Commanding General of Walter Reed Army Medical Center; and Col. L. Mauri Flitcher, Director of the Army Prosthetics Research Laboratory.

Working together, Mr. Nielson and Mr. Clare L. Milton, Jr. of Baltimore developed a process for the manufacture of a cosmetic glove which can be fitted over a prosthetic hand provided for amputees or can cover hand injuries that leave disfiguring scars. The glove can be made to match the wearer's own hand in color and skin texture and all line markings and contours of a normal hand can be duplicated. In addition, natural hairs or nylon threads can be added to the glove to imitate its natural appearance. The glove is made by pouring plastic into a negative mold of a model hand. Pigmentation is then added to conform to the hand to be matched.

The inventors have assigned rights to the Government of the United States to manufacture and use their process for government purposes without payment to them of any royalty.

## ARMED FORCES MEDICAL SYMPOSIUM



Doctor Edward H. Cushing, Deputy Assistant Secretary of Defense (Health and Medical), headed a group of more than 200 senior military medical officers and civilian physicians, shown above, who attended the Armed Forces Medical Symposium at Sandia Base, New Mexico, from 6 to 10 January 1958. The medical symposium was especially designed to orient medical service officers of the Armed Forces concerning special medical problems and the most current special weapons information. In addition, the latest developments in the application of atomic energy and a discussion of the related medical problems in the field of nuclear research were presented. The program was arranged under the direction of Colonel Lawrence B. Hanson, MC, USA, Staff Surgeon of the Armed Forces Special Weapons Project. It is planned that similar courses will be held in the future in order that the most recent developments on the biological and medical aspects of the atomic age may be disseminated widely throughout our armed services.

## Reviews of Recent Books

**MEDICAL DEPARTMENT UNITED STATES ARMY** *Surgery World War II*  
*Orthopedic Surgery in the Mediterranean Theater of Operations* by  
*Oscar P. H. M. J. M. D. F. A. C. S. C. I. MC. USAR* 368 pgs  
 Illustrated by the Chief Clerk of the Medical Department  
 for Orthopedic Surgery with the Chief Clerk of the Medical  
 Department of the Army Medical Service  
 Office of the Surgeon General Department of the Army Washington 25  
 D. C. 1957 First by the Special Department of the U. S.  
 Government Printing Office Washington 25 D. C. Price \$4

This volume is a record of tribulations encountered in the care of wounds involving bones and joints in the early days of the fighting in North Africa and of the surgical principles and technics that were eventually evolved. Much of this knowledge that was gained by trial and careful evaluation of the results had been evolved on a limited scale in the closing phases of World War I and then forgotten. This book and the companion volumes from the other theaters are our best insurance that these sound principles and technics will be available right from the beginning of any future hostilities.

The section on initial surgery of compound fractures is especially rewarding. It describes the treatment from first aid and resuscitation through the actual technic of wound excision or debridement in a manner that should be understandable to the inexperienced who will use this manual as a guide. It describes the reparative phase of surgery the object of which is to convert an open wound to a closed one within 10 days of the initial débridement. Other sections deal in a similar fashion with wounds of joints and with amputations.

About half of the book is devoted to the management of regional problems such as fractures of the humerus, both bones of the forearm and wounds of joints, and the description of the technics that were evolved for their management. This is the best manual detailing the management of skeletal wounds that I have seen. The illustrations are numerous, well chosen, and well reproduced. This book should be on the shelves of all surgeons. —WILLIAM S. STRYKER, Capt. MC. USN

**PRINCIPLES OF SURGICAL PHYSIOLOGY** by Henry A. D. M. D.  
 C. M. F. A. C. S. F. W. D. by L. R. D. G. T. D. M. D. F. A. C. S.  
 841 pgs. Illustrated by P. L. B. H. B. I. Med. I. Book Dept. of  
 H. P. & B. N. W. Y. N. Y. 1957 Price \$20

This complete work constitutes a compilation of the physiologic concepts in a surgical frame of reference. In no other book have I been able to find such a broad and yet detailed treatment of the various concepts of surgical physiology and biochemical facts. The contents are arranged in two parts: General Principles and Systemic Physiology. It has an excellent and complete index and a useful appendix of values and formulas which enhance the value of this book as a quick reference for the busy surgeon.

Part I includes all the general physiologic problems. The presentation on water electrolytes and acid base balance tends to be tedious as is the case with almost all such detailed and technical information. The mastery of this section is extremely important in the proper treatment of radical extenterations, enterocolitis, and fistulae. If one feels an acute lack of information regarding physiologic anesthesia, he will find here a clear and precise discussion of the surgeon's responsibilities. The effects of operative trauma are clear and pertinent. Many conditions requiring surgery are analyzed in regard to the advantages and disadvantages of the accepted positions on the operating table.

Part II is in brief a review of the systemic physiology. Each chapter is short yet surprisingly comprehensive in the description of pathologic states and their inherent physiologic derangements. The treatment of the circulatory dynamics in the various congenital cardiac lesions, including catheterization data and clinical findings, is as lucid as I have ever seen. Liver function tests, differential diagnosis of jaundice, and various surgical problems, including partial hepatectomy and shunting procedures, are meticulously described in the chapter on liver and bile ducts. The treatment of hepatic insufficiency omits the use of glutamate, preparatory enemas, potassium salts, and 10 per cent carbon dioxide. The urinary tract is amply discussed with commendable portions on the process of micturition and the genesis of nephrolithiasis. The nervous system section is well balanced, and the discussion and the diagrams of neuroanatomy and the effects of the various lesions are good in that the most esoteric landmarks are omitted.

This book is recommended as a guide for all surgeons and would be especially useful in residency training programs. It should also be included in the library of the physician in other fields who thinks physiologically and appreciates this necessity in his practice.

—RAYMOND A. LAWN Col USAF (MC)

**J A M A CLINICAL ABSTRACTS OF DIAGNOSIS AND TREATMENT**  
Published with the Approval of the Board of Trustees *American Medical Association*. 564 pages. Intercontinental Medical Book Corp. with Grune & Stratton, Inc. New York, N. Y. 1957. Price \$5.50.

The editor of this volume has presented the medical profession with a collection of abstracts selected from those published during the year 1956 in the abstracts section of the *Journal of the American Medical Association*. He states in the preface that he selected those abstracts which he considered to pertain most directly to the two most important aspects of clinical medicine—diagnosis and treatment. The large quantity of current world literature makes abstracting services useful and important. Additional culling of abstracts already published in a widely read journal is a somewhat different approach to the problem. The service in the *J A M A* is good and widely disseminated; several journals have very fine abstracting services.

and excellent independent services are available all of which give amazingly rapid abstracting service. The particular criteria of selection mentioned by the editor and organization of the material according to anatomic systems which is used in this collection will no doubt appeal to some although this will depend on the philosophy of the individual physician. The book is modestly bound and the format resembles that used in the abstracts section of the *J A M A*. The index is adequate. —JOHN K. SPITZNAGEL M D

ESSENTIALS OF CLINICAL PROCTOLOGY by M I G Spesm M D  
B S L L D F I C P d L s M l w M D B S F A C S  
3d d t Gun & St tto I c N w Y k N Y 1957 P r e \$8 75

As the title implies this is a short concise review of the more common diseases and deformities of the anorectal region. One chapter devoted to Coccygodynia and Proctalgia Fugax calls attention to a condition frequently overlooked. The book compares favorably with others of its kind by different authors. It could readily be recommended for senior medical students, interns, and the practitioner who performs proper proctologic examinations with occasional surgery.

—GEORGE M LYNCH C pt MC USN

NEW RESEARCH TECHNIQUES OF NEUROANATOMY A Symposium Sponsored  
by the National Multiple Sclerosis Society edited by W H M F  
W dl Ph D S D Fo w d by F d k L St Ph D 98  
p g l l t ted Charl C Th ma P bl h Sp gf ld Ill  
1957 P r e \$4 75

The techniques discussed in this symposium include tissue culture, electron microscopy, silver impregnation of degenerating axons, silver staining of synaptic terminations, radioautographs for measuring blood flow in various areas, quantitative histochemistry and histochemical localization of cholinesterases. From the usual approach of devising different staining techniques, a new method emphasizes synaptic endings while another provides for better determination of fiber terminations as well as for comparison with sections stained by other procedures. From the younger art of tissue culture it appears as though normal activity of both neuron and sheath cell are necessary for myelin formation. It also appears as though the action of serotonin or lysergic acid diethylamide (LSD) has an appreciable effect on the pulsatile function of oligodendrocytes. Electron microscopy discloses detailed structures within cells plus the structural relationship of cells to each other.

A more deviant device called radioautography reveals blood flow in gray matter to be faster than in white matter and further reveals different functional areas of cat cortex to have different rates of blood flow. Toward the latter part of the symposium there are presentations which deal with histochemical techniques. Through substrates and inhibitors data concerning localization and function of the cholinesterases is obtained. Microscopic quantitative histochemistry may

open even greater vistas. Knowledge obtained from implementation of these technics is presented in a clear and concise manner so that either the devotee or neophyte may readily learn about recent advances in the field of neuroanatomic research. The bibliography enhances acquisition of this information —ARTHUR J. LEVENS, Lt Col MC USA

**HYPOPHYSECTOMY** edited by O H Pearson M D F A C P American Lecture Series Publication No 315 A Monograph in The Bannerstone Division of American Lectures on Tumors edited by David A Karnofsky M D 154 pages Charles C Thomas Publisher Springfield Ill 1957 Price \$5

Those interested in obtaining information concerning the relatively new procedure of hypophysectomy will find in this monograph a comprehensive appraisal of the status of hypophysectomy by surgical and radiological methods. The results of treatment of patients with cancer of the breast, other types of malignancies, and with vascular complications of diabetes mellitus by hypophysectomy are detailed by investigators who have become recognized authorities in this field. The physiologic effects of removal of the pituitary gland are presented. Details of management of the hypophysectomized patient during and after surgery are given.

An interesting feature of this monograph is the presentation at the end of each of the four chapters of the questions, answers, and comments that arose during discussions by the participants to the conference from which the material for this monograph originated. It should be read by everyone concerned with the management of patients who have cancer of the breast —GEORGE F. PEER, Col MC USA

**METHODS OF GROUP PSYCHOTHERAPY** by Raymond J Corsini Ph D 251 pages illustrated The Blakiston Div McGraw-Hill Book Co Inc New York N Y 1957 Price \$6 50

This book is a comprehensive review of group psychotherapy, apparently the first of its kind, directed to practitioners and students of the helping professions: psychiatrists, psychologists, social workers, teachers, guidance workers, and others who deal with groups in therapeutic settings. The author includes the history, the various theories, and the practice of group psychotherapy in its several manifestations. He ardently subscribes to group therapy as a useful and necessary process, and emphasizes the importance of the therapist, but seems puzzled by the question of who should be a therapist and how such a person should be trained. The stress on the socioeconomic origin of neuroses in his thinking is exemplified by the following philosophical viewpoint. The writer is against psychotherapy. He wished that it did not have to exist. How much better life would be if everyone practiced mental hygiene and were so treated that no one would have those problems we call neurotic! This completely negates or ignores the biologic drives as a factor in neurotic illness. The second part of the volume gives sample records of the several

types of group psychotherapy he calls analytic nondirective psychodramatic group psychotherapy and family counseling

There is an extensive bibliography a directory of visual aids available in this field for teaching and good author and subject indexes The book is clearly written and gives evidence of the tremendous work involved in preparing such an encyclopedic volume It merits reading by anyone involved in the helping professions

—FELIX H OCKO Capt MC USN

PERIPHERAL CIRCULATION IN HEALTH AND DISEASE by W L Red h  
M D F A C P d F F T g M D B S w th  
p l t on by R L d C H S d M, D F R S E nd  
c t 154 p g llu ted G un & S tton I N w Y k  
N Y 1957 P c \$7.75

This small book is limited to the diagnostic and therapeutic approaches to the problems of the peripheral vascular system Chapters on anatomy and physiology are included Illustrations of the vascular anatomy would be much more effective than word description alone Vascular derangements are classified into three main categories acute intrinsic vascular disorders chronic intrinsic vascular disorders and vascular disorders from extrinsic causes This appears to be a practical approach The chapters on collateral circulation and venous impairment are very well written The volume represents a concise integrated approach to peripheral vascular disorders and helps to clarify thinking in this field The rather extensive bibliography offers guides for more extensive reading on the subject —JOHN B MacGREGOR Capt MC USN

THE HUMAN BRAIN Form P m t Mod m by A W L k M D  
Ph D 242 p g Ch l C Th m P bl h r Sp g f ld Ill  
1957 P c \$4.75

This book touches on an extremely wide range of subjects relating to the human brain including its development l morphologic psychologic and sociologic aspects Necessarily brief and relatively superficial discussions are included on host of subjects relating to the brain such as historical speculation on the origin of man brain anatomy and localization of cerebral functions the psychological aspects of magic religion and tribal behavior the sociologic and political problems arising as man and civilization develop and thumbnail descriptions of ancient and medieval civilizations including explorations into Greek mythology The major theme of the book written in simple and essentially nontechnical language is the development of the mind and emotions a functional psychologic and philosophic treatment rather than morphologic one Its broad coverage results in a relatively brief and superficial discussion of the many facets mentioned above The book is well written for broad and general orientation of the human brain It contributes relatively little to those already professionally oriented in the various aspects treated but contains an interesting broad coverage for those in unrelated fields

—NELSON S IRFAY Lt Col MC USA

THE PRINCIPLES OF THERAPEUTICS by J Harold Burn M A M D  
F R S 278 pages illustrated Charles C Thomas Publisher Springfield  
Ill 1957 Price \$5 50

This volume contains a series of lectures given to his students by the author who is professor of pharmacology at the University of Oxford. He succeeds admirably in linking pharmacology to therapeutics. The first few chapters contain a review of some primary physiologic principles and in this section there is well written chapter concerning the properties of acetylcholine. The remainder of the book is concerned with a basic review of the properties of some of the more useful of the pharmacologic agents. In these chapters are included discussions of digitalis, barbiturates, endocrine glands and their pharmacologic relations and antibiotics. Each subject is well covered in a brief manner and could be recommended for use either by a medical student or by the practicing physician. As is inevitable in a book of this type in view of the rapid advances in the field the antibiotics seem to be sketchily covered from the standpoint of today's medicine. The volume is attractively bound and has an excellent index. A few pertinent references are listed at the end of each chapter. This book may serve for review purposes for the medical student or for the practicing physician who desires a brief discussion of the subject of pharmacology and its relation to therapeutics at a rather basic level.

—JOHN E GORMAN Capt MC USN

THE CLINICAL ASPECTS OF ARTERIOSCLEROSIS by Seymour H Rinzler  
M D F A C P 339 pages illustrated Charles C Thomas Pub-  
lisher Springfield Ill 1957 Price \$8 75

The purpose of this volume is to assemble under one cover the necessary information needed for a practicing physician to understand, diagnose and treat the degenerating disease state of arteriosclerosis. The first chapter on general considerations attempts to clarify basic investigations of a morphologic, physiologic, biochemical, geopathologic and epidemiologic nature. The author stresses the accepted generalized nature of this disease and then tends to take sides on the highly controversial dietary vagaries which can be slanted in either direction by the authors quoted. This problem may or may not be urgent, however. I for one feel that individual emotions and the scientific competition among investigators should not be allowed to affect our thinking on this matter.

The cardiac aspects of arteriosclerosis is included in a chapter devoted to the anatomy and diagnosis (including tests designed to elucidate latent disease) of the coronary arteries. The following chapter on differential diagnosis of chest pain is rather brief and does not elaborate on the truly clinical evaluation of sectional pain.

The chapter on treatment of effort angina contains only medical therapeutic agents and covers briefly the usual drugs and a wide variety of other agents such as vitamin E, cytochrome C, x-radiation



**In this issue**



*Oliguria*

*Chemopallidectomy*

*Effective Vector Control*

*Acute Radiation Syndrome in Man*

*Iliac Bone Grafts for Cranial Defects*

*Hepatic Cirrhosis versus Lupus Erythematosus*

**SERVICE ARTICLES   ☆   REVIEWS OF NEW BOOKS**

**CLINICOPATHOLOGIC CONFERENCE   ☆   CASE REPORTS**

# UNITED STATES ARMED FORCES MEDICAL JOURNAL

*Published Monthly by  
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## Monthly Message

There are three types of research (1) basic (2) applied and (3) developmental

1 Fundamental discoveries are often made at almost no monetary cost. They are the result of acute observation of the trained mind—Withering's recognition of the value of digitalis Jenner's observation of the protection of vaccination in smallpox Fleming's discovery of penicillin

2 Good examples of applied research based on the background of fundamental and furthered by developmental research are the discovery of the value of liver in pernicious anemia and insulin in diabetes

3 The development of penicillin is an excellent example of the application of both applied and developmental research to the fundamental observation of Sir Alexander Fleming. This was directed by the Office of Scientific Research and Development. Another example much in recent news is the successful launching of the Russian satellite. The Soviet Government is to be sincerely congratulated on this accomplishment. This shows clearly what can be done when a major effort is made in applied and developmental research. It should be an example to all of the results produced by intensive directed and developmental research. The early fundamental observations of Albert Einstein and Niels Bohr solved the splitting of the atom. Money did not buy this but has since been required in vast amounts for further applied and developmental research.

Money alone does not ensure results and the value of the basic observation may not be realized for years. The sulfonamides, penicillin, barbituric acid and its derivatives, smallpox vaccination.

About 400 million dollars were expended on medical research in the United States last year from all sources. This is a gross approximation yet with a total medical bill of 15 billion dollars research accounted for about 2.7 per cent of the whole. Quite apart from methodology, research trains the mind in accurate observation, proper evaluation of observations and findings and in the ability to recognize the unexpected so that the unanticipated result or even accident, may be fruitful of further experiments and observation. This has been called serendipity. The recognition of such fortuitous or even apparently damaging results

often extends research into new fields. It is unrealistic to consider research as a series of closed compartments. There must be relationship and fluidity among all types, and provision should always be made for continuity and adjustment when further exploration is indicated.

Almost as a corollary, one might consider an axiom true throughout history that any discovery of worldwide importance often is arrived at spontaneously in several areas simultaneously. Such results can never long be kept secret in one group or area, and furthermore, the dispersion of this knowledge is in direct proportion to the number of people involved.

*Frank B. Berry*

FRANK B. BERRY, M.D.  
Assistant Secretary of Defense  
(Health and Medical)

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## Foreword

The United States Army Medical Journal is published bimonthly by the Surgeon General's Office, Department of the Army, Washington, D. C. It is the official journal of the Army Medical Department and is the principal source of information for the medical profession in the Army. It is published by the Surgeon General's Office, Department of the Army, Washington, D. C.

FRAZER BERRY M D

Assistant Secretary of Defense (Health and Medical)

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Surgeon General, United States Navy

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Surgeon, United States Army

# UNITED STATES ARMED FORCES MEDICAL JOURNAL

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## EVALUATION OF INFLUENZA VACCINE IN AN EXPLOSIVE EPIDEMIC OF MIXED ETIOLOGY

JONAS E. SALK, M.D.  
ADAM J. RAPALSKI, Colonel MC USA

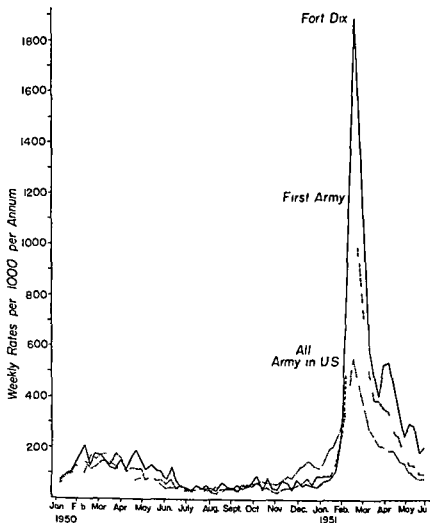
A SERIES of studies of influenza and influenza like disease has been in continuous progress at Fort Dix, N. J. since the fall of 1947. These studies, conducted under the auspices of the Commission on Influenza of the Armed Forces Epidemiological Board, have been carried out with the support of the Office of the Surgeon General, Department of the Army, in collaboration with the medical staff of this installation and with the active participation of the First U. S. Army Medical Laboratory. A considerable volume of information has been gathered in the course of these studies relating to the problem of vaccination against influenza and to the broader problem of the etiology of influenza like respiratory disease.

It had been our intention to put together a continuous story for the period 1947 to 1954; however, it has not been possible to make a full report and because of the current interest in the influenza problem we have summarized some observations made during one of the more severe outbreaks—the one that occurred in the winter of 1950 to 1951. Clinical studies carried out during this outbreak are being reported by Lerro Rapalski and Schmer-

From the Virology Laboratory, University of Pittsburgh School of Medicine, Pittsburgh, Pa. and the Medical Service, Fort Dix, N. J. Col. Rapalski is now Chief, Preventive Medicine Branch, Medical Station, Headquarters, U. S. Army Europe, APO 403, New York, N. Y.

Studies reported by the Commission on Influenza, Armed Forces Epidemiological Board, Washington, D. C.

An outbreak of influenza that was part of a widespread prevalence in the United States and other countries began rather suddenly at Fort Dix at the end of January 1951 and reached a peak after the middle of February. A comparison of the intensity of the Fort Dix experience with that of the First Army area of which Fort Dix is a part and that of all Army installations in the continental United States is shown in figure 1. This chart illustrates the difference in the prevalence of respiratory dis-



Figur 1 H p t l adm f fl en a d c mm p atory d  
1950 1951

ease in corresponding periods of 1950 and 1951 and emphasizes the impact of the epidemic at this installation in comparison with an Army area command and with the Armed Forces in the

continental United States. The probable reason for the relatively greater severity of the outbreak at Fort Dix will become apparent from data to be presented. Nevertheless, the abruptness of the episode is clearly shown, and its force is evident from the number of cases that occurred in a relatively short period of time.

The daily admission rates for influenza and other acute respiratory diseases during this period, are shown graphically in figure 2 which reveals the fluctuations in admission rate, with week end troughs followed by Monday peaks. These variations are not evident in the relatively smooth curve of the epidemic curve described by the weekly admission rates (fig. 3). The columns in this figure compare the epidemic period of 1951 with the corresponding period of 1950 to show the excess morbidity resulting from the infectious agents prevalent in 1951.

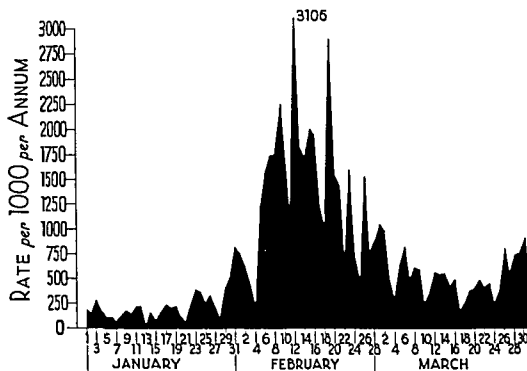
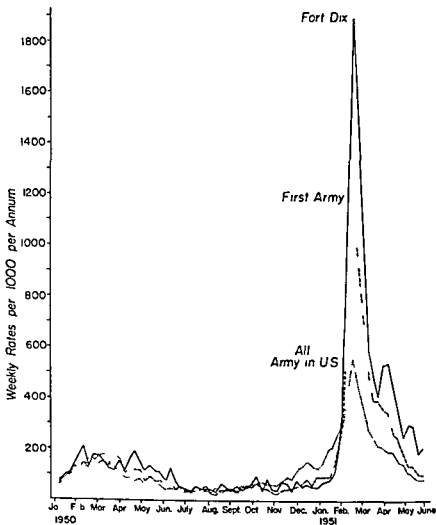


Figure 2 Daily admissions to U. S. Army hospital for respiratory diseases first quarter 1951

From the relative smoothness of the epidemic curve revealed in figures 1 and 3 it seemed reasonable to presume that a single etiologic agent was operative. That this was not the case was revealed in the course of studies on vaccination against influenza which were then in progress. These studies suggested that if a single etiologic agent was operative and if the agent was an influenza virus, it was only remotely related antigenically to the antigen in the vaccine. Alternatively, it was possible that more than one etiologic agent was in circulation.



An outbreak of influenza that was part of a widespread prevalence in the United States and other countries began rather suddenly at Fort Dix at the end of January 1951 and reached a peak after the middle of February. A comparison of the intensity of the Fort Dix experience with that of the First Army area of which Fort Dix is a part and that of all Army installations in the continental United States is shown in figure 1. This chart illustrates the difference in the prevalence of respiratory dis-



Figur 1 H p t l adm f fl nd mm p at ry d  
1950 1951

ease in corresponding periods of 1950 and 1951 and emphasizes the impact of the epidemic at this installation in comparison with an Army area command and with the Armed Forces in the

TABLE 1 *Results of serologic studies for influenza during outbreak at Fort Dix N J in January to March 1951*

Month	Proportion of cases studied serologically		Proportion serologically positive for influenza A	
	Number	Per cent	Number	Per cent
January	234/344	68.0	47/234	20.1
February	2186/2401	91.0	782/2186	35.8
March	985/1096	89.9	124/985	12.6
Total	3405/3841	88.6	983/3405	28.0

Numerator = Number of cases studied serologically  
 Denominator = Number of admissions for respiratory diseases including influenza and all forms of common respiratory diseases

Numerator = Number of cases positive for influenza A  
 Denominator = Number of cases tested serologically

lescent serum samples were tested simultaneously. The antigens used in the serologic test were PR8 and FM1. A group of negative and positive paired serum samples were tested with the epidemic strain and revealed no significantly increased sensitivity in diagnosis. Only 35.8 per cent of the 2186 cases studied that occurred in February, and only 12.6 per cent of the 985 cases studied that occurred in March were influenza A. The probable reason for the relatively low rates of serologically positive cases of influenza and for the disparity between the rates for February and March are suggested by an examination of figure 4.

The curves in figure 4 are derived from data on those cases in which paired acute and convalescent blood samples were available, and were constructed using the device of 7 day moving rates to smooth out the irregularities resulting from wide daily and week end fluctuations in admissions. It is evident that a serologic diagnosis of influenza was made in a few cases in early January and a significant number at the end of January, then a sharp rise to a peak occurred prior to the middle of February, with an equally sharp decline followed by a small number of scattered cases in March and April.

The curve describing the rate of occurrence of cases that were serologically negative for influenza reveals a rise beginning at about the same time as did the curve for influenza, but the rising limb of the curve was a trifle more gradual and reached a peak approximately 15 days after the influenza peak. The declining limb also seems to have been a bit more gradual than for the influenza curve and there occurred a second wave in late

March and early April. These data suggest that another etiologic agent was operative in addition to the virus of influenza A and that it induced disease clinically indistinguishable from influenza A.

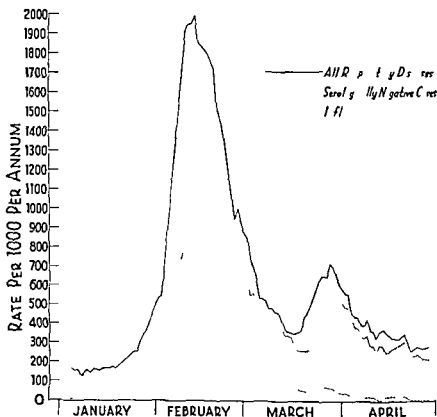


Fig. 4. Serological data from the outbreak of influenza A virus in the United States, 1951.

Although attempts were made by inoculation of chick embryos, suckling mice and other animals to identify the presence of an agent other than influenza virus, no attempt was made to isolate a virus by tissue culture methods. Subsequently, Hilleman and co-workers and Rowe and associates, using tissue cultures, identified the agents now included in the adenovirus group. Although we would have liked to have been able to report that one or more of the adenoviruses was responsible for the cases that could not be identified as having been caused by the influenza virus, it is not possible to do so because the material collected from the Fort Dix outbreak has not yet been restudied from this point of view.

The absence of this information has been responsible in part for the delay in making this report. However, the information

available is of interest even in the absence of a specific answer to this question, because there is strong circumstantial reason for believing that the adenoviruses, or agents that behave like them, contributed to the pattern observed. It was noted that the cases that were serologically negative for influenza occurred principally among new recruits, as is characteristic of adenovirus disease in military installations, whereas influenza virus disease was fairly widely distributed, both among new recruits and seasoned troops. Among 685 unvaccinated trainees admitted to hospital during the outbreak, 269 were diagnosed serologically as influenza A, and 416 were negative in this respect, among 600 operating personnel who were admitted during the same period, the ratio was reversed, with 382 positive for influenza A and 278 negative. It is probable that the concurrent outbreak among recruits of a disease not caused by the influenza virus, contributed to the greater intensity of the "influenza" outbreak at Fort Dix, which was a recruit training center, as compared with the remainder of the First Army area and with the Army in the United States (fig. 1).

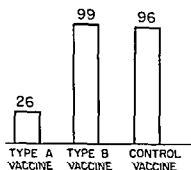
The predominance of the noninfluenza virus disease among trainees is revealed further by comparison of the frequency of occurrence of influenza A and the influenza like syndrome in trainee groups in which vaccination studies were carried out. In the vaccination program, by a method of random selection one third of the population was given a type A virus vaccine, one third received a type B vaccine, and one third received a formalinized salt-solution preparation for control. The type A vaccine contained 500 CCA units per ml, and was comprised of equal parts of PR8, FM1, and the Cuppett strains. The type B vaccine also contained 500 CCA units but was made up only of the LEE strain. The influenza viruses isolated from this outbreak were not greatly different antigenically from the Cuppett strain incorporated in the type A vaccine then under study.

The results of the vaccination studies are summarized in figure 5. Comparisons between vaccinated persons and controls are made separately for cases in which a diagnosis of influenza A was made serologically and for cases of influenza like disease that could not be shown by serologic methods to be caused by any of the known influenza viruses. There were approximately an equal number of cases of influenza A in the groups given type B vaccine (99 cases) and control material (96 cases). This is as expected. In the group given type A vaccine only 26 cases were observed. This would suggest a degree of vaccine effectiveness of more than 70 per cent.

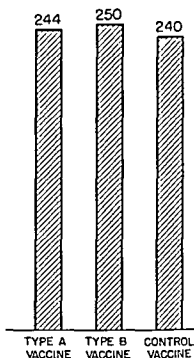
The significance of this is enhanced by the concurrent observations of distribution of vaccinated and controls among cases of respiratory disease that could *not* be diagnosed se-

rologically as influenza A. It is evident that the frequency of this illness was approximately the same in groups given type A vaccine, type B vaccine, or control material; therefore influenza vaccine had no effect upon the incidence of this disease. However, it also is evident that the relatively lower incidence of influenza A in the type A vaccinated group is not an artifact due to the use of the criterion of serologic diagnosis which could conceivably favor the vaccinated group. If the latter criticism applied, then one would have expected an excess in the type A column for the serologically negative cases.

INFLUENZA A  
Serologically Positive



INFLUENZA-LIKE  
Serologically Negative



Fort Dix January-April 1951

Fig. 5. Distribution of influenza A and of an influenza-like illness by type of vaccine.

It is clear that an evaluation of the efficacy of influenza vaccination without reference to the etiologic nature of the illness during the presumably "pure" influenza A epidemic of 1951 would have resulted in a conclusion of essentially no vaccine effect if the ratio of the combined heights of the two sets of columns were considered whereas an analysis of the

effect of vaccine against the specific disease revealed more than 70 per cent effectiveness in prevention of influenza A

### DISCUSSION

Without the serologic data, one might have gained the impression that vaccination was essentially without effect especially if the total number of influenza and influenza like illnesses were indiscriminately considered together in attempting to evaluate the effectiveness of the vaccine

There is little question from these data that the complete control of influenza and influenza like illnesses in military recruits at least, requires a combined vaccine that includes not only the influenza viruses but also those responsible for the clinically indistinguishable illnesses that can occur independently or simultaneously with influenza virus outbreaks. It is now possible to protect against the noninfluenza virus disease that is almost indistinguishable from it and caused by adenoviruses, since it has been demonstrated that vaccines for the prevention of such diseases are effective<sup>4</sup>

The question of immunologic differences among strains of influenza virus is not yet fully resolved and will not be until more years have gone by. Nevertheless, it would seem possible that stability of antigenic composition can begin to be approximated by including all strains, as may have occurred in the past in an emulsified vaccine preparation<sup>5</sup>. It may be necessary to reinforce such basic immunization<sup>6</sup> and to add new strains to the vaccine but this may be sufficient to reduce the extent to which small outbreaks become large at least those outbreaks due to viruses related to the antigens present in such vaccines. While it is clear that protective measures have been devised for the control of influenza and adenovirus infections, all of our theoretical and technical knowledge is yet to be fully applied.

### SUMMARY

Data are presented showing that a sharp outbreak of "influenza" at Fort Dix N. J. in January, February, and March 1951, was caused by the almost simultaneous activity of influenza A virus, and another etiologic agent that seems to have behaved like adenovirus in a recruit training center. During the height of the epidemic only about one third of the cases were due to influenza A virus infection. Evaluation of the efficacy of influenza vaccine based on clinical rather than serologic diagnosis would have resulted in the conclusion that the vaccine had essentially no effect, whereas in fact a single 1 ml dose of vaccine, containing 500 CCA units of the type A strains (PR8, FM1, and Cuppett) reduced by more than 70 per cent the frequency of hospital admissions for influenza A.

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*Phy an* 70 81-90 1957

# THERAPEUTIC COMPARISON BETWEEN AUREOMYCIN AND APC IN CLINICAL INFLUENZA

SANTINO J LERRO *Colonel MC USA*

ADAM J RAPALSKI *Colonel MC USA*

FREDERIK SCHMERER *Major MC AUS*

**D**URING an explosive epidemic of "influenza" at Fort Dix, N. J., in February 1951 247 consecutively hospitalized patients were placed in a special study group in an attempt to resolve conflicting reports as to the efficacy of Aureomycin (brand of chlortetracycline) in the treatment of influenza.<sup>1-3</sup> This epidemic was found by Salk and Rapalski<sup>4</sup> to have been caused almost simultaneously by influenza A virus and an agent that behaved like an adenovirus.

## MATERIALS AND METHODS

From 6 to 10 February, the Admitting Officer of this hospital alternately placed patients admitted with clinical influenza in Study Groups A and B. When admissions to the study groups were closed it was learned that the names of three patients admitted to Group A had been duplicated and that of a total of 247 patients in the study 122 were in Group A and 125 in Group B.

The patients in both groups were given yellow capsules of similar appearance four times a day. The contents of the capsules were not known to the ward medical officers or ward personnel, but were known to the Chief and Assistant Chief of the Medical Service and the hospital pharmacist, who distributed them to the wards in containers labeled "Flu Capsules A" and "Flu Capsules B." Capsules A, which were given to patients in Group A, contained 250 mg of Aureomycin. Capsules B, for patients in Group B, consisted of approximately 420 mg of APC powder (acetylsalicylic acid 200 mg, acetophenetidin 170 mg, and caffeine 50 mg). A margarine coloring agent was added to capsules B to give them the same appearance as capsules A.

From the Medical and Preventive Medicine Service, U. S. Army Hospital, Fort Dix, N. J., in collaboration with the Fort Dix Field Study of the Commission on Influenza, Armed Forces Epidemiological Board, under the supervision of Jonas E. Salk, M. D., University of Pittsburgh. Col. Lerro is now Senior Medical Advisor, U. S. Army Advisory Group, APO 102 San Francisco, Calif.



The patients were examined at least twice daily by the ward medical officers and were seen once each night by the Chief and Assistant Chief of the Medical Service. Throat and sputum cultures, roentgenograms of the chest, blood counts and determinations of cold agglutinins and erythrocyte sedimentation rates were obtained whenever possible for each case. If the patient developed unusually severe or untoward symptoms, he was dropped from the study group and given additional treatment as indicated. Patients developing complications were moved to a special ward for closer supervision and treatment.

## OBSERVATIONS

As shown in table 1, 59 of the 247 cases originally admitted to the study were dropped either because they developed complications or inadvertently received other treatment or because definite serologic data were not available. Of the 188 cases remaining in the study, 97 were in Group A and 91 in Group B.

TABLE 1. Distribution of the 247 cases originally admitted to the study and as follows: dropped from the study and as follows:

Reason for dropping	Group A		Group B		Total	
	Number	Percentage	Number	Percentage	Number	Percentage
Developed complications	3	1.2	7	2.8	10	4.0
Received other treatment	2	0.8	13	5.3	15	6.1
Definite serologic data not available	4	1.6	3	1.2	7	2.8
Total dropped	16	6.4	11	4.2	27	10.9
Total remaining in study	25	10.1	34	13.7	59	23.8
Remaining in study	97	39.3	91	36.9	188	76.2
Original cases	122	49.4	125	50.6	247	100.0

Three of the original 122 cases in Group A were dropped because of complications, two having developed otitis media on the third hospital day and one having been shown to have primary atypical pneumonia. Seven of the original 125 cases in Group B were dropped for complications. Three of these had primary atypical pneumonia (one also developing myocarditis subsequently), three had acute follicular tonsillitis, and one had otitis media on admission.

The fact that only 1.2 per cent of the group receiving Aureomycin were dropped because they developed complications as compared with 8 per cent of the group receiving APC capsules is interesting but not statistically significant. The Chi square

for this difference is 1 7706, or a P of slightly less than 0.2 and the observed difference could be ascribed to chance.

The 15 cases dropped from the study because they received other treatment included several treated by ward surgeons because of concern over hectic temperatures or suspicion of pneumonia, and two in which subsequent history revealed administration of antibiotics in the outpatient clinic during the 24 hour period prior to admission. The confused serologic data that caused the elimination of seven cases resulted from recent vaccinations for influenza.

Although influenza and the simultaneously occurring influenza like syndrome could not be distinguished clinically, serologic studies (table 2) proved that of the 188 cases retained in the study 112 were influenza A, with exactly half of the proven cases in each of the two study groups. As shown in table 3, there was no significant difference in the distribution of maximum temperatures during the first five hospital days between the cases of serologically positive influenza A and those of the influenza like syndrome.

TABLE 2 Serologic findings on the 188 cases retained in the study

Serologic findings	Group A		Group B		Total	
	Number	Percent	Number	Percent	Number	Percent
Positive for Influenza A	56	29.8	56	29.8	112	59.6
Negative for Influenza A	41	21.8	35	18.6	76	40.4
Total	97	51.6	91	48.4	188	100.0

Data presented in table 4 show the mean numbers of days of illness prior to hospitalization, mean number of days of hospitalization, the per cent of the patients having a preceding history of upper respiratory infection, the per cent with acute onset, the mean maximum temperature in hospital, mean duration of fever in days, mean white blood cell count, and mean erythrocyte sedimentation rate. In neither influenza A nor in the influenza like syndrome was there any significant effect to be noted between those treated with Aureomycin and those treated symptomatically with APC capsules.

The mean maximum temperatures for the first five days of hospitalization by treatment group for both diseases, as presented in table 5, shows no significant difference in the fever course of either treatment group. This is further illustrated in figure 1.

TABLE 3 D mb / 188 mpt t d by mmt mp tur bydy / t l b p l d y

T mp ur ( F )	T 1 l 1						1 fl						S 1 z						lly p						fl						1 t						1 fl						1 k ynd m					
	1	2d	Dy	Dy	3d	4h	5h	Dy	Dy	4h	5h	Dy	Dy	2d	Dy	3d	Dy	4h	5h	Dy	Dy	2d	Dy	3d	Dy	4h	5h	Dy	Dy	2d	Dy	3d	Dy	4h	5h	Dy												
N mb f																																																
97	1	4	8	23	19			1	4	3	11	10		0	0			0	0		5	12		9																								
98	0	15	35	57	79			0	11	22	36	50		0	4			0	4		13	21		29																								
99	15	51	68	71	65			9	28	41	43	35		6	23			6	23		27	28		30																								
100	23	42	36	23	13			16	25	21	11	9		7	17			7	17		15	12		4																								
101	44	24	18	7	2			23	15	10	5	1		21	9			21	9		8	2		1																								
102	59	24	14	1	2			33	13	8	1	0		26	11			26	11		6	0		2																								
103	30	16	5	2	0			17	7	3	1	0		13	9			13	9		2	1		0																								
104	8	7	0	0	0			7	5	0	0	0		1	2			1	2		0	0		0																								
105	2	1	0	0	0			2	0	0	0	0		0	1			0	1		0	0		0																								
106	1	0	0	0	0			0	0	0	0	0		1	0			1	0		0	0		0																								
T 1	183	184	184	184	180			108	108	108	108	105		75	76			75	76		76	6		75																								
N d	5	4	4	4	8			4	4	4	4	7		1	0			1	0		0	0		1																								



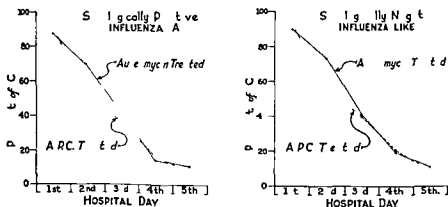
TABLE 4. Characteristics of patients with influenza A and influenza-like syndrome by group

	Influenza A		Influenza-like		Syndrome	
	Group A	Group B	Group A	Group B	Group A	Group B
Number of patients	56	56	2	41	35	6
Mean age (days)	23	16	19	2	2	9
Mean duration of illness (days)	1	7.5	7.4	0	1	6
Percentage of patients with fever	4	35.7	1	34.2	5.4	4
Percentage of patients with cough	73.2	4	23	0	0	6
Percentage of patients with sore throat	11	1	21	3	11	1
Percentage of patients with rhinorrhea	6	2.9	2	4	4	2.6
Percentage of patients with conjunctivitis	84.0	77.5	3	9.6	1	59
Percentage of patients with lymphadenopathy	9	12.9	1	11.1	10.6	1.5

TABLE 5. Maximum temperature (F) by hospital day of illness

Hospital Day	Influenza A		Influenza-like syndrome	
	Group A	Group B	Group A	Group B
1	101.6	101.4	101.9	101.4
2d	100.5	99.0	100.6	100.3
3d	99.5	99.4	99.5	99.4
4th	98.8	98.7	98.7	98.7
5th	98.4	98.5	98.6	98.5

which shows the per cent of patients with maximum temperatures over 100 F on respective hospital days. Over 50 per cent of the patients in both groups no longer had temperatures of 100 F or more by the third hospital day.

Figure 1. Distribution by time of day of patients with maximum temperature  $\geq 100^{\circ}\text{F}$ .

## DISCUSSION

The data presented show that with the dosage of Aureomycin used in this study (250 mg four times a day) as compared with APC capsules (420 mg four times a day) there was no difference in the course of the two diseases, which appear to have been caused by different etiologic agents. The dosage of Aureomycin we employed was less than that used by Finland and co workers<sup>2</sup> in their smaller series of cases, but was comparable to the dosage used by Thalmann and associates.<sup>4</sup>

The present study was limited originally to an evaluation of the effects of Aureomycin as compared to APC capsules in the treatment of uncomplicated clinical influenza. All patients in either of the study groups who developed pulmonary or other serious complications were dropped from the study. When the study was completed and the results of serologic tests for influenza became available, it was evident that we were dealing with two clinically indistinguishable disease entities, namely influenza A and an influenza like syndrome.

Table 1 shows that of those cases retained in the study group, about 60 per cent were caused by an influenza A virus. Although data as to the mean number of days of hospitalization are included, no conclusions based on these data should be made because these soldiers were discharged from the hospital only when they were fit for duty. All of the other data are significant, in that they show that neither with serologically positive influenza nor the influenza like syndrome is there any appreciable difference between the treated groups for any of the categories listed.

## SUMMARY

During a sharp outbreak of clinical influenza at an Army installation, 247 consecutively admitted cases were placed in a study group to determine the effectiveness of Aureomycin on clinical influenza. The 122 patients in Group A were treated with Aureomycin capsules, 250 mg four times a day. The 125 patients in Group B were treated with APC capsules containing acetylsalicylic acid, 200 mg, acetophenetidin, 170 mg, caffeine, 50 mg, and a yellow coloring agent. Any patient who developed complications or appeared to be acutely and severely ill was excluded from the study. For this and other reasons only 168 cases were retained in the study.

When the results of tests on acute and convalescent blood sera were reported, it was learned that we were dealing with two disease entities, namely influenza A and an influenza like syndrome. In the latter disease the usual serologic tests for influenza and also virus isolation attempts were negative.

The results showed that in this series of cases Aureomycin in the dosage employed had no significant effect as contrasted with APC on the clinical course of uncomplicated proven influenza A and on the influenza like syndrome

ACKNOWLEDGMENT Th sho g t f l t C I I W l l m B F t r  
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#### ARTIFICIAL RAIN MAKING

Among the witch doctor fraternity rainmaking is often an important activity but it does not appear in the curriculum of the modern medical student To that extent perhaps we must put it down as a lost medical art However it has engaged the attention of the physical scientists in recent years

Artificial rainmaking is unlikely to be of economic importance unless methods are available which can be applied easily and cheaply on a wide scale It is no use relying on methods which involve treatment of individual clouds Silver iodide released from aircraft remains active at cloud level for several hours in daylight and for a much longer time at night It can readily be dispersed over a very wide area This provides a method which can be applied for practical rainmaking At the same time the fact that silver iodide can successfully induce rain to fall from suitable cloud systems does not necessarily mean that there will be an increase of rainfall over an area if the process is repeated a large number of times The possibility exists that in each case the clouds might have rained naturally if left alone for a little longer

—EDITORIAL from Current Comments

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# UNUSUALLY SEVERE CASES SEEN IN AN EXPLOSIVE EPIDEMIC OF INFLUENZA AND INFLUENZA LIKE SYNDROME

SANTINO J LERRO *Colonel MC USA*  
FREDERICK SCHMERER *Major MC AUS*  
ADAM J RAPALSKI *Colonel MC USA*

**A**N acute epidemic of what appeared clinically to be influenza developed at Fort Dix N J, in the latter part of January 1951 and reached a sharp peak in February. Serologic studies reported by Salk and Rapalski<sup>1</sup> showed that the epidemic was of mixed etiology, being caused by the nearly simultaneous activity of influenza A virus and an agent that behaved like one of the adenoviruses subsequently described by Hilleman<sup>2</sup> and Rowe<sup>3</sup> and their associates.

During the period 1 January through 31 March, more than 3 400 patients were admitted to the U S Army Hospital at Fort Dix. The vast majority showed only those symptoms usually seen in mild cases of influenza, including chills fever malaise generalized aches and pains, sore throat congested nares persistent cough profuse perspiration and weakness. In these cases the illness ran a short febrile course followed by rapid and complete recovery. A small number of the patients however, were severely ill, with various debilitating complications and prolonged convalescence.

In 0 88 per cent of the 3 400 cases there was pneumonia with delayed resolution despite adequate chemotherapy, in 0 12 per cent there was myocarditis, which often appeared late in the course of the illness or during convalescence. The following four cases illustrate these special features.

## CASE REPORTS

**Case 1** An 18 year old man who had been ill since 20 January with a common cold was admitted to the hospital on 2 February because

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From the Medical and Postgraduate Medicine Services U S Army Hospital  
Fort Dix N J in collaboration with the Fort Dix Field Study of the Committee  
on Influenza and the Armed Forces Epidemiologic Board under the sponsorship of  
E S L M D University of Pittsburgh Pittsburgh Pa. Col Lerro is now Senior  
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of acute illness and the finding of coarse rales throughout both lung fields. Physical examination on admission revealed dullness and numerous moist rales over the right lung field posteriorly and in the right axilla. The remainder of the admission findings and a summary of the complete course in the hospital are shown in figure 1.

This was a case of serologically proven influenza A complicated by bilateral pneumonia with a severe prolonged hectic febrile course showing no response to multiple antibiotic and sulfonamide therapy. There was delayed resolution of the pneumonia and *Monilia albicans* was recovered from the sputum following the intensive use of antibiotics.

It is not possible to state with certainty that this was a bacterial pneumonia despite the finding of pneumococci in the sputum. The organisms were not subjected to a Neufeld typing and may have represented a nonpathogenic variety of pneumococcus rather than one of the virulent strains. It is noteworthy that the patient's fever and pulmonary involvement were not influenced by extensive use of antibiotics resulting in suppression of the normal bacterial flora of the throat. This suggests that the influenza virus may have a severe prolonged pathogenicity of its own even if secondary invaders are suppressed; however, it is not possible to exclude the fact that moniliasis may have contributed to the patient's symptomatology in the latter phases of his illness. The employment of vigorous supportive measures such as oxygen therapy and maintenance of fluid balance along with good nursing care is shown to be of prime importance in the management of an illness of this type.

C 2 A 22-year-old man who had been increasingly ill with what appeared to be mild influenza since 2 February was admitted to the hospital on 9 February with the symptoms listed under that date in figure 2. Shortly before admission he had developed vomiting and some dizziness. Figure 2 summarizes the complete hospital course.

In this case of serologically proven influenza A complicated by bronchopneumonia there was prolonged high fever, mental confusion and cerebral delirium and eventual electrocardiographic findings compatible with myocarditis. There was no apparent response to antibiotics and sulfonamides. Occasional pneumococci were found in the sputum culture taken on admission but none in the blood culture.

C 3 A 22-year-old man was admitted to the hospital on 11 February for a respiratory condition of four days' duration. He appeared acutely ill and there was dullness and bronchial breathing over the right chest anteriorly. Figure 3 lists his symptoms on admission and presents a summary of his complete course while hospitalized.

This patient had serologically proven influenza A complicated by pneumococcal pneumonia as evidenced by lobar consolidation seen in roentgenograms of the chest, a high white blood cell count and the presence of pneumococci in the blood stream. Despite intensive

Date in Feb. 51	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	APR 11
Day of Hospital	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	67
Day of Illness	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27	79
Temperature																
Chloromycetin Gm/day orally	05 1 1 2 1 Total 55 gm															
Penicillin Units x 10 <sup>6</sup>	06 12 12 12 12 Total 258 million U 27 million U daily															
Triple Sulfas Gm/day	6 6 5 Neutropenia Total 17 gm															
AUREO Gm/day orally	3 2 1 Total 23 gm															
Streptomycin Gm/day IM	Total 11 gm 1 2 gm daily 1 1															
Aspirin gm/day	2	3	3	3	Total 11 gm											
Symptoms	Chills Fever Cyanosis of lips Nausea Appetite fair Productive cough & tenacious yellow sputum Flushed face Headache continues Productive cough & thick yellow mucus Sore throat Severe productive cough & bloody expectoration Prostration Alert and cheerful Stuffy nose Pharyngitis Tonsillitis Profound prostration Sleeping at short intervals Med rales of rt LL & axilla Med rales of rt LL & axilla Med rales of rt LL & axilla Flushed face Headache Prostration															
Oxygen	+ + + + + + + +															
ECG	21 Feb Normal 2 March Normal															
WBC x 1000	49 50															
Sed. Rate mm/hr.	34															
Blood Culture	Sterile Sterile Sterile															
Sputum Culture	Neisseria α Strep No acid fast Monilia Albicans Negative for Monilia Albicans Pneumococci bacilli H Influenza															
Chest X Ray	2 Feb 7 Feb 19 Feb 26 Feb 															

Fig 1 Consol dated hospitalizat on cha t case 1 infl en a A and bilateral pneumon a.

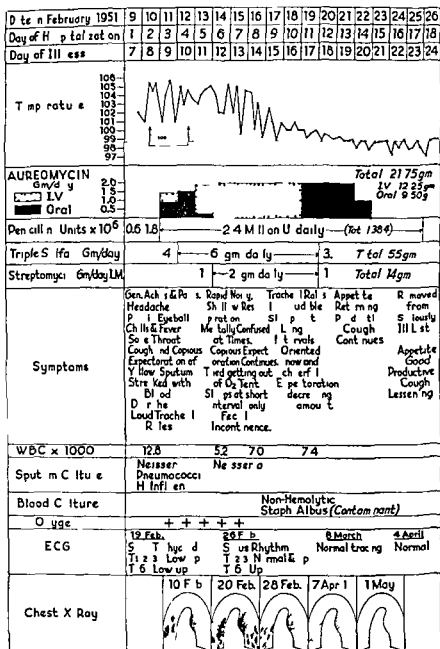


Figure 2 Continued hospitalization chart as 2 file Auth  
b b p m la a d m y a d i s t i s.





course in hospital is presented in figure 4. Serologic study of acute and convalescent blood sera revealed no significant rise in antibody titer for influenza.

This patient had a severe influenza like syndrome soon complicated by pneumonia and later by myocarditis. The pneumonia developed on the ninth day of illness after four days of treatment with penicillin and Chloromycetin. Multiple antibiotic and sulfonamide therapy had no clinically observable effect on either the influenza like syndrome or the pneumonia and pneumococci still could be recovered from the sputum after prolonged treatment with penicillin Aureomycin Chloromycetin and triple sulfonamide. During the later stages of the patient's illness there was electrocardiographic evidence of myocarditis as manifested by development of ST T changes. This persisted for over a month but was followed by complete recovery.

### DISCUSSION

These four cases are representative of the relatively small number in which influenza A or the influenza like syndrome assumed a severe and malignant form, or in which there were serious complications. To a variable extent there was pulmonary infiltration with notably delayed resolution, prolonged hectic fever, severe prostration with impending circulatory collapse, and electrocardiographic evidence of myocarditis. Lymphadenopathy appeared in a large number of cases and in an occasional case there was splenomegaly.

#### Myocarditis

This was an important though infrequent complication. A tachycardia while at rest in a patient (case 2) who was hospitalized early in the epidemic, caused us to re-examine his cardiovascular system. An electrocardiogram revealed ST T wave changes compatible with myocarditis. It could not be determined when during the course of his illness this patient had developed the myocarditis and after one week the ST T waves returned to normal.

In view of this finding and of the report by Finland and associates<sup>4</sup> of two cases of influenza with post-mortem findings of acute nonbacterial myocarditis, we obtained electrocardiograms on all patients during the remainder of the epidemic who developed complications, had an unusual clinical course or developed persistent tachycardia, particularly if it occurred late in the course of the illness or during convalescence.

Myocarditis also occurred with the influenza like syndrome as illustrated by case 4. This patient had a persistent tachycardia throughout his illness. Serial electrocardiograms revealed only sinus tachycardia until the 24th day of his illness, when ST T wave changes compatible with myocarditis were noted.

The ECG findings gradually returned to normal over a period of six weeks after which progressive ambulation was permitted. No cardiovascular sequelae were noted upon his discharge to duty.

An important observation in this epidemic was that a previously healthy young soldier with influenza A or the influenza like syndrome could have such a serious complication as myocarditis late in the course of the illness or during convalescence with a resting tachycardia as the only clinically suggestive sign. Had electrocardiographic studies not been done this complication would not have been recognized and therefore not treated. Out of a total of 3 400 cases of clinical influenza seen during the epidemic there were 4 (0.12 per cent) with myocarditis. No specific therapy was given these four patients except bed rest with bathroom privileges only until the ECG returned to normal thereafter a gradual return to full activity was carried out. No complications developed subsequently to our knowledge.

#### Pneumonia

The incidence of pneumonia (all types) with x ray confirmation in this epidemic was 0.88 per cent. There generally was a marked delay in resolution despite intensive use of antibiotics. This is well illustrated in cases 2 and 3. In both cases the pneumonia had not completely cleared even two months after onset. In these two cases the temperature remained normal after the antibiotics were discontinued in spite of the continued presence of pneumonic infiltration.

#### Fever

In uncomplicated cases the temperature ranged from 101 to 104 F for three to five days with return to normal by crisis or lysis and an afebrile course thereafter. There was no discernible difference in the effect of Aureomycin and of APC (aspirin, phenacetin and caffeine) on the duration or degree of fever in these patients. A few cases showed unpredictable swings of temperature with elevation for one or two days then a drop to normal for four or five days and then a sudden elevation and subsidence only to be repeated some days later. Cases of this type were screened carefully for complications. Occasionally a roentgenogram of the chest revealed a pneumonic infiltration for the first time following such a flare up in temperature. The medical staff quickly became aware of the deceptive character of the temperature curve in clinical influenza and remained on the alert for relapses during the patient's convalescent period.

### Prostration

There often was profound weakness during the first days of illness, but this generally decreased after two to three days. Many of the soldiers, with the phenomenal recuperative powers of youth, would rebound from a state of hyperpyrexia, extreme lethargy, and weakness on the day of admission to exuberance, high spirits, and impatience at remaining away from their units, in the brief space of three or four days. However, post-influenzal asthenia was present in noteworthy degree in an occasional patient. It was necessary to retain these latter patients in the hospital until the asthenia had completely disappeared, before their return to duty.

### Role of Antibiotics

It was our impression that neither antibiotic nor chemotherapeutic agents in any combination had any specific effect in altering the course of these diseases. In some instances, after about ten days of fever despite the use of combinations of antibiotics a drop in temperature followed the addition of another antibiotic but this might have been coincidence. It is our belief that the influenza virus has a pathogenicity of its own for which no appropriate medication is available at present, and that the treatment must consist of employing sound medical principles of therapy, good nursing care, supportive measures, and constant vigilance of the patient to recognize complications as they arise.

In case 1, the use of a combination of antibiotics suppressed the normal bacterial flora of the respiratory tract so completely that a pure culture of *M. albicans* was obtained. The patient continued to run a protracted severe, febrile course, and it is possible that moniliasis may have contributed to his symptomatology in the latter phases of his illness. Several observers have reported that with extensive use of antibiotics and suppression of the normal bacterial flora of the respiratory tract pulmonary moniliasis may develop.<sup>6</sup> This is one of the hazards of the prolonged use of antibiotics in large doses.

### Laboratory Studies

Routine throat and sputum cultures taken during this epidemic revealed a wide variety of organisms, including neisseria, pneumococci, alpha streptococci and *Hemophilus influenzae*. Because the latter has been noted frequently in epidemics of influenza we compared its relative prevalence in sputum and throat cultures for the first quarters of 1950 and 1951 respectively. As shown in table 1 only 8.9 per cent of the cultures taken in the first quarter of 1951 were positive for *Hemophilus influenzae*, as compared with 12.9 per cent for the first quarter



of 1950. A random sampling of 10 blood specimens taken for heterophil antibody studies showed a titer of 1/112 in four cases of 1/224 in four cases of 1/448 in one case and of 1/3584 in one case. In all except this last case which proved to be one of infectious mononucleosis the titer dropped on absorption with guinea pig kidney and with boiled beef cells especially with the guinea pig kidney absorption test. In the last case the titer after absorption with guinea pig kidney was 1/1792 and after absorption with boiled beef cells was negative.

TABLE I Comparison of the prevalence of heterophil infection in throat and sputum cultures at Ft Dix, 1st quarter of 1950 and 1st quarter of 1951

	1950				1951			
	Jan	Feb	Mar	Total	Jan	Feb	Mar	Total
Number of throat cultures	15	7	23	45	137	203	123	463
Number of sputum cultures	14	13	13	40	64	93	35	192
Total	29	20	36	85	201	296	158	655
Number of positive throat cultures	2	4	5	11	21	31	6	58
Number of positive sputum cultures	6.9	20.0	13.9	12.9	10.4	10.5	3.8	8.9

### Results of Treatment

No deaths occurred in our series of approximately 3,400 cases of clinical influenza in contrast to the large number of deaths in older people noted in the 1951 epidemic in the area of Liverpool, England. While the vigor and youth of our group of patients were factors of prime importance in determining the favorable course of this particular epidemic, careful medical observation, good nursing care, and prompt institution of supportive measures including oxygen and parenteral fluids played an important role in facilitating the recovery of the seriously ill patients.

### SUMMARY

In a series of approximately 3,400 cases of influenza A and an influenza-like syndrome hospitalized during an explosive epidemic of mixed etiology in early 1951 at Ft Dix, N. J., a few cases assumed an unusually severe and malignant form. Myocarditis, an important though infrequent complication, appeared late in the course of the illness or during convalescence in 0.12 per cent of the cases. Pneumonia with markedly delayed resolution despite intensive use of antibiotics and chemotherapy

occurred in 0.88 per cent. In one of the four cases presented, moniliasis developed as a consequence of antibiotic therapy. Neither antibiotics nor chemotherapeutic agents had any specific effect in altering the clinical course, nor was there any salutary effect from any combination of drugs; however, no deaths occurred in this series of 3,400 cases in which the most effective treatment given proved to be nursing and prompt supportive measures.

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**ACKNOWLEDGMENT** The authors wish to thank Colonel William B. Foster, MC, USA; Lt. Colonel James L. Hansen, MC, USA; Lt. Colonel Andrew Fodor, MSC, USA; Lt. Colonel Warren N. Christopher, MSC, USA; and Major John P. Dwyer, MSC, USA, for their cooperation and assistance in this study.

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# RAPID DETECTION OF ORGANIC BROMIDES IN BIOLOGICAL FLUIDS

GEORGE R. NAKAMURA M. S.

**T**HE UREIDES (*e. g.* bromisovalum and carbromal), next to the barbitrates are the most common sedatives found in toxicological specimens submitted to this laboratory. Several methods are available for the estimation of bromides in biological specimens. They depend on the determination of bromides or bromine by iodometric titration or by color formation with gold chloride or rosaniline. These procedures have useful applications; however, for toxicological identification a more rapid technic was sought for the analysis of bromides in biological fluids, usually in gastric washings, urine, and blood.

This laboratory has adapted Feigl's spot test for inorganic bromine for the identification of organic bromide. The method depends on the formation of red eosin from yellow fluorescein when the latter is exposed to bromine vapor.

The extraction and fusion methods of previously described identification procedures for bromisovalum and carbromal were adapted for use in detecting these organic bromides in biological specimens. Because ureides are classified among weak acids or non acids, the extraction is performed just below neutral pH.

## METHOD

To a separatory funnel, introduce 10 to 50 ml of fluid specimen and add to it five times the volume of chloroform. Then add a few drops of 10 per cent HCl to adjust the pH to about 5 to 6 using a pH indicator paper. Shake the funnel for five minutes. Filter the chloroform extract through Celite (Johns Manville) into a beaker and evaporate on a hot plate until almost dry.

Collect the residue by dissolving in ethyl ether and transfer it to a 10 by 75 mm Pyrex or other borosilicate glass tube. Dry the ether extract in the tube by gentle heating in a water bath. Mix approximately three times the amount of solid sodium carbon

F m 406 h M d l G l L bo ry APO 343 S F C l f Mr N k  
mur w U S Army M l ry P l L b ry d R p y F E APO  
343 S F an C l f

ate thoroughly with the residue and heat the mixture in a hot flame until decomposition is complete. Plunge the bottom of the hot tube into 5 ml of water contained in a small beaker and stir the mixture. Cool the solution and acidify it with an excess amount of glacial acetic acid.

Transfer the entire amount of the solution into a 50 ml Erlenmeyer flask. Add to the solution about 10 mg of lead peroxide powder. Close the mouth of the flask with a sheet of filter paper impregnated with fluorescein (0.1 per cent in alcohol), and bind with a rubber band. Apply freshly dried, impregnated paper.

Prepare a reagent blank and a standard in the same manner. Use a small amount of potassium or sodium bromide as a standard, 20 to 50  $\mu\text{g}$  of bromine is a convenient working range.

Warm the flask gently on a hot plate for about five minutes. Depending on the amount of bromine present, a circular red fleck of varying intensity is formed on the yellow test paper at varying periods of time after the beginning of the heating process.

#### DISCUSSION

The speed with which the circular red fleck appears, depends on the concentration of bromine. Table 1 shows the rate of the appearance of red eosin color. The minimum amount that can be detected by this method is 10  $\mu\text{g}$  of bromine, provided the fluorescein solution is prepared fresh from time to time. A solution that had been kept on the shelf in this laboratory for six months could detect only a minimum of 30  $\mu\text{g}$  of bromine.

TABLE 1 *Typical rate of appearance of eosin color*

Micrograms of bromine	Time in seconds
500	15
200	20
100	45
50	60
20	100
10	120

Measured from the beginning of the heating process

There is no significant loss of bromide when a bromide sodium carbonate flux is heated over a high temperature burner (700 to 800 C). This was confirmed by fusing a known amount of bromide (10 to 50  $\mu\text{g}$  of bromine) with sodium carbonate, and measuring the rate with which the converted eosin appeared on the paper in comparison with standard bromine samples that were not fused.

Natural constituents in biological fluids including normally occurring traces of bromine, do not interfere with this test, nor do some of the compounds that occasionally occur in acid chloroform extracts such as salicylates phenobarbital amobarbital hexobarbital acetanilid and acetophenetidin

### SUMMARY

A rapid and simple procedure is described for the detection of organic bromides in biological fluids Feigl's technic for the spot test of inorganic bromine has been adapted for organic bromide identification

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### CAN MEDICINE PREVENT WARS?

We obviously have had a large influence on the growth and development of medicine and surgery Can medicine come to have an influence in thwarting the occurrence of wars? I believe it can and should take steps to wield its influence in helping to bring about a warmer spirit of wanting to understand our fellow man in other areas of this troubled world No remedy can equal the solvent action of unfeigned sympathy in dispelling the perplexing anxieties cares and vexations of life When will the nations of this earth come to consider themselves as one people whose fortunes rise or fall with any others?

—OWEN H VANGENSTEEN M D

*J Am IL t*  
p 402 N 1957

# THE DETERMINATION OF SERUM CHOLESTEROL

## Use of Liebermann Burchard Reagent in Zak Procedure

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ELLIS R. PUGH *Airman First Class USAF*

**I**N 1954, Zak and co-workers<sup>1</sup> described a procedure for serum cholesterol wherein color was developed by adding a concentrated sulfuric acid solution of ferric chloride after the alcohol acetone filtrate had been evaporated in a conical centrifuge tube and the residue taken up in glacial acetic acid. Although analytically satisfactory in experienced hands, the Zak technic is objectionable on three grounds:

1. Extreme care is necessary in order to avoid accidents in the repetitive pipetting of comparatively large volumes of sulfuric acid.

2. Even minor charring at the acetic acid color reagent interface as the latter is added will result in errors that are difficult to detect in the presence of the normal deep purple shading.

3. The color reagent must be either prepared daily (time consuming because ferric chloride dissolves in sulfuric acid with difficulty), or it must be thawed after being stored in the deep freeze. Both alternatives result in delay.

In an effort to avoid such objections, we decided to apply the Liebermann Burchard reagent to the Zak procedure. This reagent meets all three requirements in that it requires considerably less volume sulfuric acid, is completely compatible with acetic acid, obviating the possibility of mixing errors, and can be freshly prepared daily in a few moments. The complete technic as practiced in this laboratory has been evaluated over the past 18 months.

## PROCEDURES

## Equipment

- 1 Volumetric flasks, 25 ml glass stoppered
- 2 Pipettes volumetric transfer, calibrated to deliver 1 ml Ostwald Folin 0.5 ml
- 3 Buret 10 ml with 0.5 ml graduation
- 4 Filter paper Whatman No 41 made fat free by washing with ether and drying
- 5 Glass stirring rods approximately 3 mm outside diameter and 6 inches long
- 6 Cuvettes for Beckman model B 1 cm light path 1.5 ml capacity
- 7 Funnels and 50 ml Erlenmeyer flasks

## Reagents

- 1 *Alcohol ether mixture* 3:1 Mix 3 volumes of 95 per cent alcohol (U S P) with 1 volume of anhydrous peroxide free ether (AR)
- 2 *Glacial acetic acid* (99.5 per cent U S P) Must be clear and free of extraneous material
- 3 *Acetic anhydride sulfuric acid reagent* 20:1 Place 20-40 or 60 ml of cold acetic anhydride in a dry well stoppered mixing cylinder and slowly add 1, 2, or 3 ml respectively of cold concentrated sulfuric acid Mix with care by repeated inversion Cool until the temperature of the reagent is between 23 and 25 C Use within 1 hour
  - a Acetic anhydride (ACS)
  - b Sulfuric acid concentrated (ACS) Must be colorless

Component parts of the color reagent are stored in a refrigerator to speed cooling of the reagent before use

4 *Cholesterol standards*

- a Stock standard = 1 mg cholesterol/ml Place 500 mg of freshly recrystallized free cholesterol in a 500-ml volumetric flask dissolve in glacial acetic acid by heating if necessary cool to room temperature and dilute to volume with same
- b Working standards (S 0.1 mg/ml S 0.2 mg/ml S 0.4 mg/ml) Into three 50-ml volumetric flasks pipet respectively 5, 10 and 20 ml of stock standard dilute to volume with glacial acetic acid Should be prepared fresh every two or three weeks

### Technic

1 Place approximately 15 ml of alcohol ether mixture into a 25 ml volumetric flask and add 1 ml of serum or plasma from a transfer pipet, drop by drop, while agitating the flask

2 Heat flask to boiling in a water bath dilute almost to volume with alcohol ether mixture allow flask to come to room temperature

3 Dilute to volume with alcohol ether, stopper, and mix by shaking and inversion

4 Filter through fat free Whatman No 41 filter paper into a 50-ml Erlenmeyer flask, draining off last drop by touching lip of volumetric flask to filter paper

5 Immediately pipet 1 ml aliquots of the filtrate into two conical, 15 ml, centrifuge tubes

6 Evaporate aliquots to dryness in a hood, using dry air and heat from an infrared heat lamp (fig 1) Remove from heat as soon as they are completely dry Samples may be covered and stored at this point

7 To each tube add 0.5 ml of glacial acetic acid from a buret place a glass stirring rod in each tube and mix to ensure complete solution

8 Place 0.5 ml glacial acetic acid into another centrifuge tube for use as a blank pipet 0.5 ml of each of the three working standards in duplicate into centrifuge tubes place a stirring rod in each tube

9 Add 1 ml of freshly prepared and cooled acetic anhydride-sulfuric acid reagent to the blank and first three tubes mix with the stirring rod, and place tubes in a 25° C, light tight water bath add reagent to three tubes every 2 minutes and treat as above (The order in which the tubes are colored is not important as long as they are read in the same order as colored)

10 Transfer samples to cuvettes and read  $\sigma$  T setting blank at 100% T in a Beckman model B spectrophotometer at 660 millimicrons (red tube) exactly 45 minutes after addition of coloring reagent

*Note* Care must be taken to exclude moisture throughout the procedure

### Calculations

Convert all  $\sigma$  T to optical densities

$$\text{Then (1) } \frac{\text{OD of standard}}{\text{mg of standard}} = \rho$$



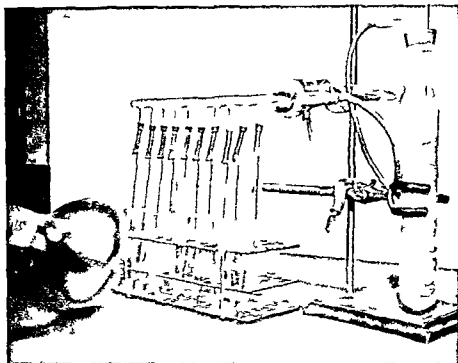


Fig 1 E apor t ion A f t b l un t h r o g h a c o t a o f d r y i n g c m p u n d (c l c i u m c h l o r i d S l a G l o D e r t ) t m o v e a l l m t u r e A t h e n d i t d t t h e m p l t b b y m o f a m a f l d u t h f t p A f a r d h a t l a m p p l a c d a b o t 6 h f m t h a m p l t b t s p d v a p a t o n.

A  $k$  value is obtained from all standards run and an average  $k$  value calculated. This value is used in calculating unknown concentrations.

$$(2) \quad \text{mg}^{\text{or}} \text{ unk} = \frac{\text{OD unk}}{k} \times 25 \times 100$$

25 = dilution factor (1 ml serum or plasma in 25 ml)

100 = factor for converting to  $\text{mg}^{\text{or}}$

#### Sample Calculations

$$(1) \quad \text{OD of S} = 0.248$$

$$\text{mg in S} = 0.1 \text{ mg}$$

$$\frac{0.248}{0.1} = 2.48 = k$$

$$(2) \quad \text{OD of unk} = 0.187$$

$$\text{mg}^{\text{or}} \text{ unk} = \frac{0.187}{2.48} \times 25 \times 100 = 188 \text{ mg}^{\text{or}}$$

If the concentration is above 350 mg%, use only 0.5 ml serum or plasma (so that % T will be within those of the standards) and double the value obtained in equation No. 2

### DISCUSSION

In those instances where a total cholesterol analysis is required, and no need for an estimation of cholesterol ester concentration exists, the primary requisites of any procedure are time and convenience. The disadvantages of the ferric chloride technic described by Zak and associates have already been enumerated. In the standard Bloor<sup>2</sup> technic the step involving evaporation to dryness in a beaker requires continued attention and care. We believe, therefore, that the procedure outlined above combines the best features of those described from the standpoint of time, convenience, and adaptability to relatively inexperienced personnel. In the course of a year and a half, at this facility, approximately 1,200 human serum samples were run on a routine basis for total cholesterol concentrations. Of these, 177 were repeated on different days and 92 were analyzed twice on the same run (duplicates). In many instances a run consisted of up to 60 samples. As indicated in table 1, the number of repeats that checked on different days within 10 per cent was 92 per cent; the number of duplicates that checked within 10 per cent was 97 per cent.

As a check on the accuracy of this method, many recovery and comparison studies were run. Recoveries of 95-100 per cent were recorded when varying amounts of cholesterol were added to serum. Comparisons with the Bloor technic have shown agreement within 10 per cent for a range of approximately 50-800 mg per 100 ml.

TABLE 1 *Variation in results on duplicate and repeat samples*

	Duplicate samples (analyzed twice on the same run)			Repeat samples (analyzed on two different days)		
	Number	Per cent variation less than	Per cent of total	Number	Per cent variation less than	Per cent of total
	66	3	72	126	5	71
	23	3.5	25	37	6-10	21
	3	6-15	3	14	11-20	8
Total	92		100	177		100

Per cent variation determined by dividing the difference between the values obtained for a sample by the average of the values.

## SUMMARY

A procedure for the determination of total serum cholesterol combining the best features of those described to date in the literature and eliminating many of the difficulties that hinder successful routine adaptation has been recorded. The convenience of this technic has been extensively evaluated over an 18 month period on approximately 1 200 serum samples

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## THE GREATNESS OF HIPPOCRATES

It must h ve been a marvelous experience to have sat under the branches of the old plane tree on the Isle of Cos listening to Hippocrates as he demonstrated his patients and following the working of a master mind. Today it may not seem remarkable that Hippocrates in making a diagnosis took the patient's history inquired carefully about his present illness his past history his family history his habit his work where he lived what he ate and drank and then made a careful physical examination employing inspection palpation and auscultation following this with a careful examination of sputum urine and stools. But in Hippocrates day soothsayers astrologers and the priests of various cults often dominated medical practice. They made their diagnoses by studying the stars by examining the organs of sacrificial animals by interpreting dreams by studying omens and portents. This makes the achievement of Hippocrates stand out in bold and dramatic relief.

—RALPH H MAJOR M D

*Lit. m. t. I R d f M d n*  
p 485 S pt 1957

# FORMATION OF MYELIN FORMS IN BRAIN TISSUE

### Fract of Surface Active Substances

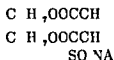
TELL (V) RE CARTER MCL

**M**YELIN FORMS are peculiar anisotropic elongated or spherical structures which are "grown" or exposures of phospholipides, ceroides and certain other lipids to water. The best known of the myelin forms are those derived from lecithin which are readily demonstrated by exposing the dried acetone precipitate of an ether extract of brain tissue to water. They have been described by Pinner as liquid crystals (paracrystals) in the mesomorphic state of matter whereas according to Fraenkel-Landolt they are not true liquid crystals but a hydration phenomenon associated with the surface-active and heteropolar characteristics of lecithin.

## EXPERIMENTS

## Formation of Myelin Forms From Brain Tissue by Means of Aerosol OT

Aerosol OT is practically pure wax like material somewhat plastic with the following chemical structure



Its properties are as follows molecular weight 444 solubility 1.5 grams per 100 ml of water at 25 C forms transparent gels at higher concentrations by the soaking out method soluble in most organic solvents pH about 6.5 in 1 per cent solution anionic and somewhat hygroscopic surface tension in 1.0 per cent solution in water 26 dynes and in 0.1 per cent solution 28.7 dynes

**Guinea Pig Brain Tissue** Ten guinea pigs were killed by intra cardiac injection of Pentothal Sodium (brand of thiopental sodium) and the brains removed. The cerebellums were discarded and the cerebrums divided into approximately equal halves by sagittal section through the corpus callosum. One half of each of the 10 brains constituted the experimental group and the other 10 halves the control group.

The brain halves in the experimental group were weighed placed separately on plate glass and emulsified with sufficient Aerosol OT to produce a concentration of Aerosol OT in each brain emulsion of 10.6 per cent. A small portion was placed on a slide and covered with a coverglass. Pressure was applied to the coverglass to obtain a thin spread before sealing with clear varnish.

The control group of brain halves was emulsified without adding any of the surface active agent and slide preparations similar to those of the experimental group were made.

Daily observations were made of both experimental and control preparations with bright field and polarizing microscopes with particular attention to the formation of myelin forms and cholesterol crystals. All preparations were at a room temperature of 23 C.

**Results** Myelin forms developed within 24 hours and persisted in all of the experimental preparations. In contrast all of the control preparations were negative for myelin forms until the 20th day when three of them became positive.

When the emulsions were first placed on a slide there was only a finely granular translucent substance visible under a microscope. Within 24 hours large oval or round spaces containing myelin forms appeared in the emulsion. Under the bright

field microscope the myelin forms were round, oval, or elongated structures with highly refractile thick or thin walls, which formed intricately tangled masses (figs 1 and 2) Under the polarizing microscope the myelin forms were anisotropic, the most brilliant anisotropy occurring in the walls when the myelin forms were spherical or when the tip of a developing myelin form was oriented in a certain way they appeared as Maltese crosses (figs 3 and 4)

Within some of the spaces in the emulsion, together with the myelin forms, there was Aerosol OT, which was opalescent homogeneous or striated, and less refractile than the myelin forms on bright field observation (figs 1 and 2) Under the polarizing microscope Aerosol OT appeared as anisotropic interlocking fan shaped plates which were either homogeneous or longitudinally striated the anisotropy was less than that of the myelin forms (figs 3 and 4) Cross striations in the myelin forms appeared on the 25th day On the 28th day of the experiment elongated myelin forms that were oriented perpendicularly to the striations of Aerosol OT appeared indicating that the molecular arrangement of the surface active agent exerted a controlling influence on the molecular arrangement of the myelin forms

It is to be emphasized that the myelin forms show dynamic growth imperceptible to the eye over a period of days In some preparations after a period of two weeks the myelin forms underwent degenerative changes indicated by loss of anisotropism and shape Myelin forms although developing preferentially in foci containing Aerosol OT, also developed in the emulsion and at its periphery

The optical sign of the myelin forms and the spherules was positive as determined with the Red I retardation plate and the polarizing microscope The positive optical sign indicates that the molecules in the myelin forms are oriented with their optic axes radially as is the myelin in peripheral nerves

In the experimental preparations cholesterol crystals formed within 24 hours in 8 of 10 emulsions whereas in control preparations a crystal was present in only one emulsion after 20 days Cholesterol crystals appeared as early as 30 minutes after the brain was mixed with Aerosol OT The crystals were flat somewhat rectangular anisotropic and under the polarizing microscope appeared to be brilliantly multicolored (figs 5 and 6) On standing the crystals increased in size

Tyrosine crystals were noted in 4 of the Aerosol OT brain emulsions on the 18th day

In the control preparations there were numerous small anisotropic structures A few myelin forms were noted in three control preparations on the 20th day Only a few were well formed (figs

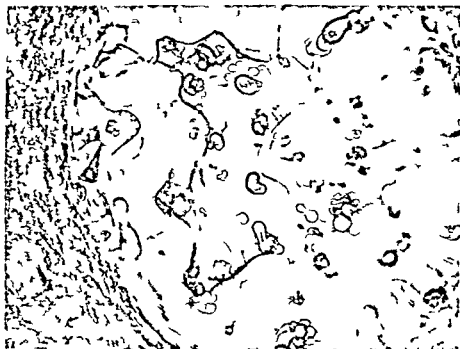


Fig 1 The myel form at the mall of the cur db d s alak of  
h mog us A ro 1 OT A ros 1 OT g a p g bra n mulston. Sev th  
d y of xp rime t ( $\times 305$ )



Fig 2 D t l of figure 1 ( $\times 630$ )



Figure 3 Same area as figure 1 photographed under the polarizing microscope. The smaller bodies that exhibit Maltese crosses are myelin forms. Aerosol OT is represented by diffusely anisotropic fan-shaped areas in the background. ( $\times 305$ )



Figure 4 Same area as figure 3 photographed under the polarizing microscope. ( $\times 630$ )



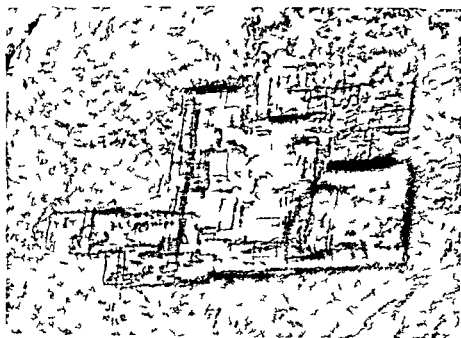


Fig 5 Chol i rol y tal A ro l OT g a p g b em l n. S tb  
d y of xp m t ( $\times 305$ )

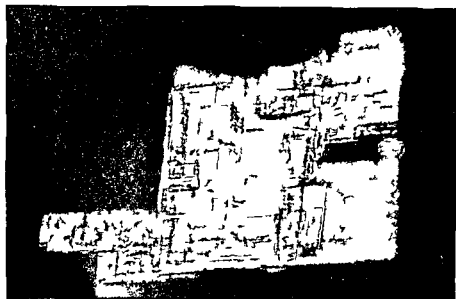


Fig 6 Sam ry tal a f g e 5 photog ph d d th p lar g m cro-  
op ( $\times 305$ )

7 and 8) The myelin forms had the same appearance as those in the experimental preparations, and formed in large spaces and at the periphery of the emulsions. No tyrosine crystals were noted. A few cholesterol crystals were present in one preparation.

**Human Brain Tissue** A fresh brain was obtained at autopsy of a white man, 24 years of age, who died from a subdural hematoma. Five grams of white matter from the corpus callosum was emulsified on a glass plate with a spatula. Aerosol OT was thoroughly mixed with brain tissue in the quantities shown in table 1.

TABLE 1 *Amounts of Aerosol OT added to human brain tissue*

Emulsion number	Amount of Aerosol OT	
	mg	"
1 (Control)	None	0 0
2	100	2 0
3	200	3 9
4	500	9 0
5	1000	17 0

A portion of each emulsion was placed on a slide covered with a coverglass and sealed as described previously. Additional preparations were made to study the effect of adding water to an Aerosol OT brain emulsion. Emulsion 5, which contained 17 per cent Aerosol OT, was diluted successively with 0.5, 1, and 2 ml of distilled water. Slide preparations were made from each dilution as previously described, and were designated as emulsions 6, 7, and 8, respectively.

**Results** Myelin forms developed in emulsions containing 2, 3.9, and 9.0 per cent Aerosol OT within 24 hours, but did not develop in emulsion 5, which contained 17 per cent Aerosol OT, or this emulsion diluted with 0.5 ml of distilled water. On further dilution of emulsion 5 with 1 ml and 2 ml, however, sparse and poorly formed myelin forms developed on the fifth and fourth day, respectively.

The myelin forms were similar to those in the Aerosol OT guinea pig brain emulsion, but were more plentiful (fig. 9). After the 5th day, and particularly in emulsions 3 and 4, the myelin forms exhibited numerous fine cross striations, were subjectively multicolored under the polarizing microscope, and completely filled or traversed spaces in the emulsion as sweeping gracefully curved structures (figs. 10, 11, and 12). Striated myelin forms of this type were found in Aerosol OT guinea pig brain emulsions only after the 25th day.



Fig 7 Myelofibrillar apparatus. The peripheral myelin sheath was intact ( $\times 30$ )



Fig 8 Same as Fig 7 photomicrograph of the peripheral myelin sheath. Two days after experiment ( $\times 305$ )



Figure 9 Myelin forms in Aerosol OT human brain emulsion No. 4. Note the difference in brilliance of the anisotropy of the myelin forms as compared to the background Aerosol OT. Fourteenth day of experiment ( $\times 305$ )

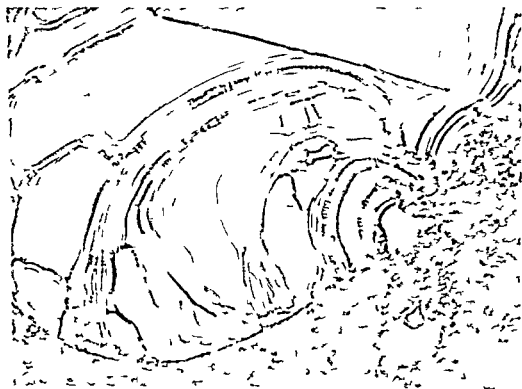
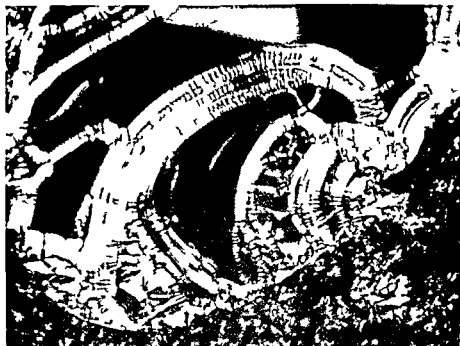


Figure 10 Myelin forms exhibiting fine cross striations in Aerosol OT human brain emulsion. In the upper portion of the illustration is a straight edge of a cholesterol crystal. Fourteenth day of experiment ( $\times 305$ )



F g 11 S m a a f g u r 10 p h o t o g r a p h d d t l p o l z g m c r o -  
c o p ( x 305 )



F g 12 S m a r f g r e 10 a d 11 b t p h o t o g r a p h d u t h u n c r d  
l d d f l t a e n t a t e r o t a t m y l f r m  
( x 305 )

Thread shaped myelin forms developed earlier than in the Aerosol OT guinea pig brain emulsions and likewise "grew" at right angles to the longitudinal striation of Aerosol OT as observed between crossed nicol prisms (figs 13, 14 and 15) When there was an abrupt change in the direction of the striation in the surfactant, myelin forms likewise changed direction, indicating control of the molecular arrangement of myelin forms by the molecular structure of Aerosol OT Myelin forms derived from human brain tissue were optically positive Aerosol OT was optically positive in the direction of its longitudinal striations, but examination of spherules of Aerosol OT indicated that in relation to the optic axes of their molecules they were optically negative

Myelin forms traversing Aerosol OT at right angles to the striations of Aerosol OT often had a color complementary to that of Aerosol OT with the Red I retardation plate in place between crossed nicol prisms that is to say, when Aerosol OT was blue the myelin forms were yellow with a reversal of these complementary colors on 90 degree rotation of the preparations With the same microscopic technic the myelin forms traversing Aerosol OT in older preparations were yellow regardless of rotation of the stage These observations suggest that Aerosol OT has the ability to determine the direction of "growth" of myelin forms and possibly to orient their molecular structure from a radial to a tangential pattern in relation to the long axis of the myelin forms

The spherules or developing tip of a myelin form exhibited a cross of polarization indicated by a dark Maltese cross against four bright quadrants With the Red I retardation plate between crossed nicol prisms quadrants 1 and 3 (upper right and lower left) were blue, while quadrants 2 and 4 (upper left and lower right) were yellow This indicated that the sign of the polarization cross was positive and that the long chains of the component molecules were oriented radially as in most fluid crystalline spherules Older spherules were laminated and multicolored with the Red I retardation plate in place (fig 16)

Aerosol OT in certain concentrations is anisotropic and must be differentiated from myelin forms It is soluble in water 1.5 grams per 100 ml and at this concentration was transparent in the bright field and not anisotropic At concentrations in water above 1.5 grams per 100 ml it was anisotropic but could readily be differentiated on bright field observation because it was almost transparent and striated longitudinally whereas myelin forms were highly refractile and had the characteristic shape previously described Aerosol OT that accumulated in spaces in the brain emulsion appeared between crossed nicol prisms as diffuse or longitudinally striated fan shaped plates which at their points of contact exhibited black or white linear areas



Fig 13 Myl f r m s d at d by th f b r g h t l a r a r r a g d p  
p d l a t l g t d l t a t f A o l O T u h b d m t a t  
n t r o l o f g r o w t h o f m y l f o r m b y A r o l O T P h o l g p h d u n d  
t h p o l n g m c r o c p u t h R d l t a r d t p l a t p l c T h i t y  
t h d a y o f x p m e n t. A r o l O T h m a b m u l i o (x 365)

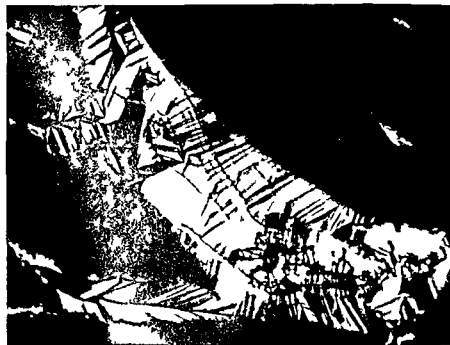


Fig 14 S m l a t f g 13 b t 80 t h d y o f x p e r m n t T h m y l f m  
d c t e d b y l a b g h t l s a m p r o m e n t A r o l O T h m  
b a e m l o n. ( 305)



Figure 15 Same area as figure 14 but photographed with green filter to accentuate the yellow lines of myelin forms. ( $\times 305$ )

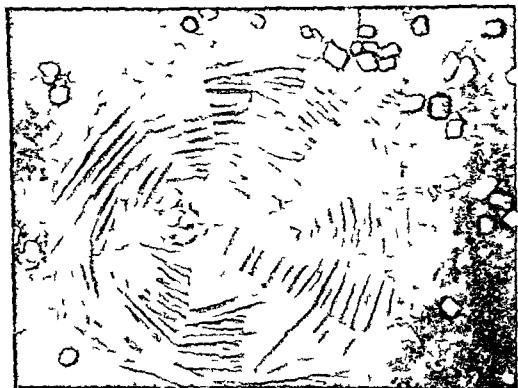


Figure 16. Myelin spherule in Aerosol OT human brain tissue emulsion No. 7. The laminated spherule is located in a lake of Aerosol OT and shows an imperfect Maltese cross. The surrounding brain emulsion contains anisotropic rectangular cholesterol crystals. Thirteenth day of experiment. ( $\times 305$ )



On dilution of Aerosol OT human brain emulsion with distilled water the difference in intensity of anisotropy of myelin forms compared with Aerosol OT was striking

Spiraled myelin forms were found in dioctyl sodium sulfo succinate human brain emulsion on the 80th day after preparation (figs 17 18 and 19)

Cholesterol crystals developed within 4 hours in emulsions 5 6 7 and 8 and in these latter within 30 minutes emulsion 5 contained 17 per cent Aerosol OT and emulsions 6 7 and 8 were dilutions of this concentrated emulsion with distilled water. No cholesterol crystals formed in control preparations of brain emulsion in 30 days or in emulsion 2 which contained 2 per cent Aerosol OT. Emulsions 3 and 4 which contained 3.9 and 9 per cent Aerosol OT respectively showed cholesterol crystals within 24 hours (table 2). The cholesterol crystals were brilliantly multicolored between crossed nicol prisms and were similar to but more numerous than those in Aerosol OT Guinea pig brain emulsions. They were particularly numerous in concentrated Aerosol OT human brain emulsions diluted with water.

TABLE 2 Form of myelin formation in human brain emulsion

Emulsion	Concentrated Aerosol OT	Day						
		4 hr	1	2	3	4	5	10
1	Non (control)							
2	2.0%							
3	3.9%							
4	9.0%							
5	17.0%							
6	Emulsion 5 diluted with water							
7	Emulsion 5 diluted with water							
8	Emulsion 5 diluted with water						++	

++ indicates to 100% crystalline preparation  
 ++ indicates undissolved crystals in preparation  
 ++++ indicates excessive undissolved crystals in preparation

With increasing dilution of emulsion 5 with water the crystals began to lose their form the corners became rounded and coloration between nicol prisms was decreased

#### Formation of Myelin Forms by Means of Various Surface Active Substances

The purpose of this experiment was to establish whether surface active substances other than Aerosol OT would form myelin forms from whole brain tissue. Their chemical structure was different but all had in common the ability to lower the surface tension of water.

Fresh dog brain was emulsified with the surfactants in the proportion of 4.5 grams of dog brain to 0.5 gram of surfactant.



Figure 17 Spiraled myelin form in Aerosol OT human brain emulsion. Eighth day of experiment Bright field. ( $\times 305$ )



Figure 18 Same as figure 17 photographed between crossed nicol prisms. ( $\times 305$ )

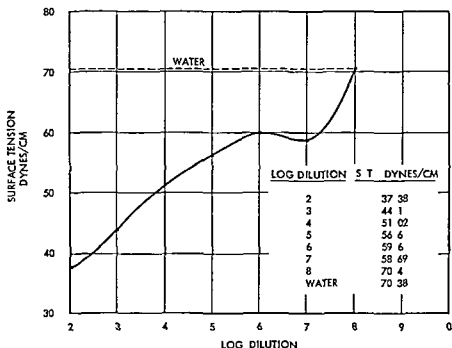


Fig. 23 Surface tension of oil of dog brain lecithin in water (action of plate of the effect of water dog brain)

#### Demonstration of Myelin Forms in the Acute Lesions of Multiple Sclerosis

Formalin fixed cerebral tissue was obtained from a 50-year-old white man with long standing multiple sclerosis who had an exacerbation of neurologic symptoms during an attack of viral hepatitis from which he died. On examination of the brain both acute and chronic lesions of multiple sclerosis were seen. Examination of frozen sections of the brain by polarizing microscopy revealed in demyelinated areas anisotropic spherulitic myelin which had the same optical properties as myelin forms produced by surfactant on brain tissue in vitro (figs. 24, 25 and 26).

#### Time Lapse Cinephotomicrography of Myelin Forms

The development of myelin forms from brain tissue by means of surface active substances and the development of myelin forms from vegetable lecithin, animal lecithin, crude dog lecithin in the presence of water and surfactants was recorded by means of time lapse cinephotomicrography. Exposures were taken at 20 second, 1 minute or 5 minute intervals. The mechanism of the development of myelin forms could be accurately determined. Some of the myelin forms grew slowly by means of coalescence of minute anisotropic bodies while others grew comparatively rapidly by the hydration phenomenon previously described. One



Figure 24 Acute lesion of multiple sclerosis. There is severe demyelination and abrupt termination of myelinated tracts. Intact neurons and infiltration with lipid-laden macrophages. Frozen section. (Hematoxylin-eosin stain  $\times 50$ )

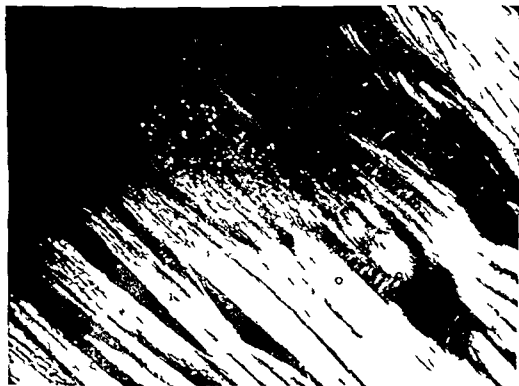


Figure 25 Similar to Figure 24 but photographed between crossed nicol prisms. An isotropic myelinated tract ends abruptly at the area of demyelination. In the transition area are spherulitic myelin forms. ( $\times 50$ )

morphic substance is placed on a freshly cleaved crystal plane it is oriented by this plane so that its optic axis always seems to place itself parallel to the cleavage plane and takes a definite direction relative to the crystallographic axes of its support. Friedel stated further that the mutual orientation is that the two lattices (single or multiple) of the two types of crystals have within a certain limit of tolerance the same form and volume orientation being impossible when the two periods are not properly matched. If one applies the observations of Friedel on mutual orientation of crystals one may speculate that there is mutual orientation of molecules between Aerosol OT and myelin forms. Myelin forms appear to have the ability to orient the molecular structure of each other as demonstrated by their helical formation when in contact. Myelin forms are similar to liquid crystals in that the molecules must have a chainlike structure not homopolar but heteropolar that is they must contain a hydrophilic and lipophilic pole. In the case of lecithin the hydrophilic group is choline.<sup>2</sup> Tyrosine crystals are apparently formed by the breakdown of proteins of cerebral tissue by the action of the surface active agent. Tyrosine is relatively insoluble in water and precipitates as crystals. We have demonstrated previously that tyrosine crystals can be formed from leukocytes liver tissue cancerous tissue and other tissues by means of a surface active agent.

Demyelination of the central nervous system is a cardinal feature of many diseases of the brain many of unknown etiology such as multiple sclerosis. Surface active substances will cause breakdown of cerebral lipoproteins with the liberation of lecithin which in the presence of water develops into myelin forms in vitro. This mechanism of myelin degeneration probably also occurs in vivo and there is direct and indirect evidence to support this view. Zunz<sup>3</sup> showed that the surface tension of plasma and serum is lowered in dogs and guinea pigs during anaphylactic shock. Weil<sup>4</sup> believed that a surface active substance derived from the liver is operative in multiple sclerosis and has produced demyelination in vitro by exposure of nervous tissue to hemolytic surface active substances as saponin and sodium taurocholate. Weil and Lulan<sup>5</sup> demonstrated a myelolytic substance in the urine of patients with multiple sclerosis. Von Muralt<sup>6</sup> demonstrated a surface active substance related to acetylcholine formed on excitation of a peripheral nerve. Nagotte<sup>7</sup> described the formation of ovoids and spheres and the closing of segment of myelin by surface tension in Wallerian degeneration of nerves. In the course of this study I have found myelin forms in acute lesions of multiple sclerosis.

The formation of spiraled myelin forms in surfactant brain emulsion is of particular interest in view of Steiner's important finding of spirochete like structures in the brain tissue of patients

with multiple sclerosis Steiner was of the opinion that he was dealing with a spirochete which he names *Spirochaeta myeloptera*, and it was the etiologic agent of multiple sclerosis. The inference is that Steiner was actually staining spiraled myelin forms which simulate spirochetes and that there is a surface active substance operative in multiple sclerosis which causes the development of spiraled myelin forms. Steiner described "spirochetes" with a knob on one end and entwined "spirochetes" similar to the helical and knobbed myelin form we have produced chemically.

### CONCLUSIONS

- 1 The addition of a synthetic surface active agent, dioctyl sodium sulfosuccinate (Aerosol OT) to unfixed human and guinea pig brain tissue causes the development of myelin forms, cholesterol crystals and tyrosine crystals in vitro. The surface active agent releases lecithin from cerebral lipoprotein which in the presence of water develops into myelin forms.
- 2 The addition of distilled water to human brain tissue containing a high concentration of dioctyl sodium sulfosuccinate causes a heavy deposition of cholesterol crystals.
- 3 The appearance and development of myelin forms under the bright field and polarizing microscopes is described.
- 4 The direction of "growth" of myelin forms is controlled by dioctyl sodium sulfosuccinate.
- 5 Helical (spirochete like) myelin forms develop from brain tissue in the presence of a surface active substance.
- 6 Dioctyl sodium sulfosuccinate in the gel state when exposed to water develops myelin form like structures some of which have a helical appearance.
- 7 Cationic, ionic, and nonionic surfactants and cobra venom cause the formation of myelin forms from brain tissue.
- 8 Myelin forms were demonstrated in the acute lesions of multiple sclerosis.

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**ACKNOWLEDGMENT** I wish to thank Frank D. Nolan, HMC, USA, for valuable suggestions and for technical assistance and Helen Knight Steward for editorial review.

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## Clinicopathologic Conference

Ireland Army Hospital Fort Knox Ky

### WEAKNESS

**Summary of Clinical History** A 30-year old Caucasian woman was admitted to the hospital with the chief complaint of extreme weakness. On the morning of 23 June 1957 she had noted weakness and was unable to stand unassisted. She remained in bed and only arose to take hot baths as treatment, but became progressively worse. On 25 June her husband took her to a civilian physician who noted that she could not hold her head erect, had difficulty in speaking and breathing, and was unable to cough productively.

By occupation the patient was an office worker. Although never constipated, she had taken two or three Ex Lax tablets daily, and, on occasion, cascara, because she "felt better" after taking them. She had had the usual childhood illnesses without complications and an appendectomy two years prior to the present illness. Six years ago she had been admitted to a hospital because of extreme weakness. There she was told that she had a potassium deficiency and was given fluids intravenously. Response to this therapy was demonstrated by an increase in strength. There had been no other similar episodes until the present illness. The past history was negative for renal disease and urinary tract disorders.

**First Hospitalization** The patient was admitted to a civilian hospital on 25 June. Her pulse was slow and irregular, her blood pressure was 130/80 mm Hg, and her temperature was normal.



Urinalysis was negative except for a trace of albumin. Hemoglobin was 16 grams per 100 ml and the red blood cell count was 4 630 000 per  $\mu$ l. There were 18 000 white blood cells per  $\mu$ l with 89 per cent neutrophils and 11 per cent lymphocytes. Spinal fluid examination was reported as normal. An electrocardiogram demonstrated flattening of the T waves in the chest leads.

The patient received intravenous fluids with added potassium chloride. Three ampules of Prostigmin (brand of neostigmine) and 0.6 mg of atropine were administered. There was no change in her condition. On the second day of hospitalization she felt slightly stronger. A roentgenogram of the chest at this time revealed a moderate amount of fluid in the right base. A repeat electrocardiogram showed frequent extrasystoles. The T waves in the chest leads were now upright.

## SECOND HOSPITALIZATION

The patient was transferred to this hospital on 26 June.

**Physical Examination** The patient's temperature was 97 F, pulse 60, blood pressure 120/55 mm Hg, and respirations were 16. The pupils were constricted but reacted to light. Ptosis of the lids was evident. The lungs were dull to percussion on the right posteriorly. There were decreased breath sounds in the same area. Frequent cardiac extrasystoles were present. No murmurs were heard. The liver was just palpable below the right costal margin, but nontender, and in the right lower quadrant an appendectomy scar was present. Edema of the extremities was not present, and the peripheral pulsations were good. Hyporeflexia was present bilaterally without pathologic reflexes. A slight brownish discoloration of the skin was noted. There was no increased pigment in the skin folds.

**Laboratory Studies** Hematocrit was 43 ml per 100 ml. The white blood cell count was 30 450 per  $\mu$ l with a differential of 89 per cent neutrophils, 2 per cent lymphocytes, 2 per cent monocytes, and 7 band forms. The corrected sedimentation rate was 17 mm per hour. Blood chemistry studies showed the following: serum potassium less than 2 mEq, serum sodium 128 mEq, and chlorides 103.6 mEq all per liter; Carbon dioxide, 9 millimols per liter; calcium 9.1 mg per 100 ml; blood urea nitrogen, 43 mg per 100 ml; and creatinine 7.7 mg per 100 ml. An admission electrocardiograph showed bigeminy from a supraventricular source and low T waves over standard and precordial leads. A roentgenogram of the chest showed a pneumonic consolidation at the right base with some pleural involvement but without evidence of effusion. The remainder of the chest appeared to be within normal limits. The spinal fluid revealed 4 white blood cells (neutrophils) per  $\mu$ l, glucose 102.5 mg per 100 ml, globulin

1 plus, protein, 61 mg per 100 ml, and chlorides, 120 mEq per liter. Urinalysis showed a specific gravity of 1.006, a trace of albumin, and was negative for sugar; there were 6 to 7 red blood cells and 1 white blood cell per high power field, and amorphous urates.

**Course in Hospital.** On 27 June fluids intravenously were instituted, with 3,000 ml of 5 per cent dextrose and water containing a total of 60 mEq KCl. This was given in the first 12 hours. By 28 June the patient appeared improved mentally, with some increase in strength but still having respiratory distress. She was taking food and fluids orally. On this date she received 1,000 ml of 5 per cent dextrose in water with 20 mEq of KCl and 2,000 ml of physiologic saline solution, the latter containing 40 mEq of potassium per 1,000 ml. Repeat blood chemistries showed a blood urea nitrogen of 65 mg per 100 ml, sodium, 134 mEq per liter, chlorides, 102 mEq per liter, carbon dioxide, 9 millimols per liter, and potassium, 1.12 mEq per liter. Repeat urinalysis was unchanged. The patient seemed to improve during the day and appeared stronger. The urinary output during hospitalization had been adequate with from 1,200 to 1,500 ml daily. Potassium by mouth was started on 27 June, and the patient received 20 mg on that day and again on 28 June. A total of 160 mEq of KCl was administered intravenously in a 48 hour period. Subsequent electrocardiograms revealed no significant change despite therapy, except for a decrease in the number of supraventricular extrasystoles. Table 1 summarizes blood chemistry findings. In the early morning of 29 June the patient's condition deteriorated. She had gasping respirations, became unresponsive, and died quietly.

TABLE 1 *Blood chemistry studies*

Chemical constituent	27 June	28 June
Sodium	128 mEq/l	134 mEq/l
Potassium	Less than 2 mEq/l	1.12 mEq/l
Carbon dioxide	9 mM/l	9 mM/l
Chlorides	103.6 mEq/l	102 mEq/l
Blood urea nitrogen	43.05 mg/100 ml	65 mg/100 ml
Creatinine	7.75 mg/100 ml	
Calcium	9.1 mg/100 ml	

## DISCUSSION

**Dr. Snyder.** My clinical impression when the patient was admitted to the hospital was that this was a case of potassium-losing nephritis secondary to either a chronic glomerulonephritis or chronic pyelonephritis. Terminal azotemia manifested by an elevated blood

urea nitrogen and creatinine was believed to be resultant from the initial disease process

The complaint of weakness the presence of hyporeflexia and the electrocardiographic changes reflected the low potassium The acidosis low fixed specific gravity hypokalemia and hyponatremia seemed to indicate tubular damage It was thought that the albuminuria and hematuria indicated glomerular damage

The lack of both a family history and periodicity along with resistance to intravenous potassium therapy tended to rule out the diagnosis of familial periodic paralysis It was evident from the protocol that the possibility of myasthenia gravis was considered The typical muscular distribution ordinarily demonstrated by this condition was not apparent however and this patient showed no response to Prostigmin Without hypernatremia hypertension and alkalosis a diagnosis of primary aldosteronism must be deleted from the differential This clinical entity does present hypokalemia that is refractory to potassium therapy as was noted in this case Collagen diseases can produce a terminal uremia However the general course of the patient was not typical of this group of diseases

In summary the hypokalemia hyponatremia acidosis hematuria albuminuria and low specific gravity of the urine together with the physical findings would indicate primary renal disease

Discussion I shall direct the discussion of the differential diagnosis in this case into that derived from the clinical picture and that from the laboratory findings It will be evident later how these dovetail and help us arrive at a conclusion as to the pathologic entity present

The prime and most evident sign and symptom: generalized weakness We can divide the various causes of this finding into several categories First under consideration would be those diseases of the nervous system producing weakness Myasthenia gravis produces weakness but primarily of eyelids and swallowing Acute infective polyn neuritis (Guillain Barre syndrome) gives generalized weakness but usually with sensory changes Poliomyelitis of course must be considered The usual picture of headache stiff neck and patchy involvement was not evident here Progressive muscular atrophy and amyotrophic lateral sclerosis produce weakness but with different distributions of involvement sporadic remissions and exacerbations

The next group of causes of extreme weakness are the infections Of course this overlaps with the previous group since infections of the nervous systems include both groups Poliomyelitis is one Meningitis is another either purulent or aseptic The stiff neck headache and fever usually present in meningitis were absent here Varieties of encephalitis can readily be excluded Of course a normal spinal

tap is of utmost importance in ruling in or out the diseases of this group

Chemical or toxic causes for weakness, as in lead poisoning are next to be considered. This is usually an isolated nerve paralysis such as of the ulnar or peroneal nerve. Tick paralysis can be included in this group. No ticks (or history of same) were present. A history of methyl alcohol ingestion was not elicited. Arsenic poisoning can give peripheral neuritis but usually with sensory changes. The next group to be included are the metabolic diseases. These would produce weakness through the production of low potassium level. This would include Addison's disease, Cushing's disease, familial periodic paralysis, and diabetic acidosis. In this case none of these fit except as we shall see shortly, that a low potassium level was present. Another important but rare cause would be "potassium-losing nephritis." Other possibilities include primary aldosteronism which gives a low potassium but high sodium level plus hypertension and edema and treatment with steroids must be mentioned. Of course chronic diarrhea is another factor to be considered in low potassium levels.

Much of the differential diagnostic possibilities mentioned can be ruled out immediately by the laboratory findings. Thus the normal findings in spinal fluid examination would tend to eliminate infections such as poliomyelitis, encephalitis, and myelitis, as well as polyneuritis. The normal sodium level eliminates Cushing's disease and aldosteronism. The most significant laboratory findings are the low potassium, high creatinine, elevated blood urea nitrogen, low CO<sub>2</sub>, and albuminuria. These certainly all point to kidney disease. I can't think of any other cause for elevated creatinine than kidney disease. This plus the other evidence of mild acidosis, albuminuria, and urea nitrogen retention indicate a very significant degree of kidney failure. Although a low potassium level as a result of potassium-losing nephritis is rare, it has been reported and seems to be a recognized entity. Without balance studies it is difficult to say if the patient was in negative potassium balance but I believe it is a safe assumption to make. It also is most difficult to make an accurate determination as to the type of kidney disease present inasmuch as all of the various chronic nephritides can produce the same end picture whether it is chronic glomerulonephritis or chronic pyelonephritis. If it were necessary to make a choice, the absence of hypertension, edema, and episodes of acute nephritis make one lean toward chronic pyelonephritis as the choice.

What was the role of the chronic use of laxatives in her death and the mechanism of death? I don't believe she died in uremia. I believe she died of potassium depletion with cardiac arrhythmia resulting therefrom. This has been discussed in an excellent paper by Relman and Schwartz<sup>1</sup> in which they pointed out the tubular abnormalities that had appeared in people who took cascara or laxatives containing aloin or phenolphthalein for prolonged periods of time and stated that

patients with chronic diarrhea from other causes such as ulcerative colitis and regional enteritis had suffered potassium depletion. Renal biopsies showed the tubular changes which they attributed to this low potassium level.

Now if we can visualize an already significantly damaged kidney losing potassium as in this case then have superimposed on it the additional insult of low potassium effect on the tubules with further damage and further loss of potassium there was then reached a point where the potassium level declined to the point at which cardiac arrhythmia and/or standstill occurred.

Dr M N M Y I would like to interject a few remarks concerning the possible basic renal lesion which existed in this patient. The excellent differential discussed by Captain Snyder in his presentation and by Colonel Deutsch leaves little room for doubt that this entity of low potassium and sodium levels along with elevated blood urea nitrogen and creatinine in an acidotic patient is renal in origin.

The kidneys as noted at autopsy definitely resembled the scarred kidneys of chronic glomerulonephritis. In retrospect a review of this patient's history does not follow the course one would expect in this disease. Here we have a patient with renal disease of at least six years' duration—if we accept the previous episode as being related and I believe we must. This implies the presence of some renal disease even prior to this. In light of this thought the absence of episodes of edema, hypertension or even clinical symptoms necessitating the seeking of medical advice during all these years is quite unusual for a patient with chronic glomerulonephritis.

For these reasons I would prefer to entertain the idea that the basic pathologic condition in the kidneys will more probably be chronic pyelonephritis. This is a disease that is common in the sex need not produce significant clinical symptoms and in fact can be mildly present in the absence of laboratory findings such as proteinuria and positive culture.

In addition there have been experimental studies as well as a few case reports where the excessive use of laxatives resulted in low potassium levels to a clinically significant degree. This has produced reversible renal changes of a hydropic nature in the proximal convoluted tubules. This patient was a chronic laxative user.

In summary I believe this patient had chronic pyelonephritis which was further insulted by a low potassium resulting from excessive use of laxatives and as a result died an electrolyte death despite attempts at restoration of potassium.

Dr C R In a child a similar clinical and laboratory picture would necessitate investigation for the possibility of poisoning with

particular emphasis upon possible arsenical nephropathy. Another disease of the nervous system producing weakness in a child is the rare disorder of amyotonia congenita. In most cases the picture of hypotonia and cardiac arrhythmia is found in hypokalemia resulting from chronic diarrhea. However, in the case under discussion I concur with the discussants' impression.

**Dr. Snyder's diagnosis**

Primary renal disease

**Dr. Deutsch's diagnosis**

Chronic pyelonephritis with potassium depletion and cardiac arrhythmia

**Dr. McNerney's diagnosis**

Chronic pyelonephritis with potassium depletion caused by laxatives

**PATHOLOGIC FINDINGS**

**Dr. Fodell:** At autopsy there was bilateral hydrothorax of approximately 1,000 ml each. The heart weighed 320 grams and showed no evident dilatation or other abnormalities grossly or microscopically. Both lungs were heavy and sectioning revealed a large amount of frothy, sanguineous edema fluid. The right kidney weighed 150 grams and the left kidney weighed 140 grams. The capsules stripped with slight difficulty to reveal a rather pronounced diffuse hemorrhagic discoloration, presumably due to cortical hyperemia rather than to petechiae. A diffuse granularity was present bilaterally. There was poor distinction between cortex and medulla with thinning of the cortical portions. The pyramids appeared pale. The pelves were not dilated and the ureters communicated normally with the urinary bladder and showed no dilatation.

Microscopically (figs. 1 and 2) the kidneys showed moderate to active pyelonephritis with chronic inflammatory infiltrates and associated cortical linear scarring. Medullary intertubular scarring and foci of calcification were present. Acute tubular degenerative changes with regeneration were widespread. Periglomerular fibrosis and fibrous obliteration of glomeruli were seen. In some areas entirely intact glomeruli were seen together with intact tubules. These areas seemed to alternate with involved areas.

The right ovary was partially replaced by a cyst which measured 1.5 by 1 cm. Sectioning revealed the contents of the cyst to be clear fluid with the cyst wall being yellow and convoluted. Microscopic study showed this to be a corpus luteum of pregnancy. Sectioning into the uterus revealed the fundic portion to be filled with a friable, polypoid material. Microscopic study showed products of conception. The adrenals had no cortical adenomata or nodularity. They were not en-

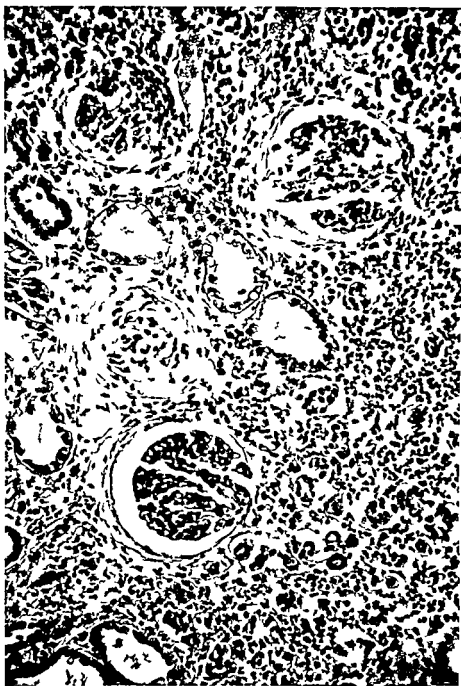


Fig. 1 Photomicrograph of tissue from kidney showing glomerular and tubular changes, including glomerular fibrosis, tubular atrophy, and tubular atrophy ( $\times 130$ )

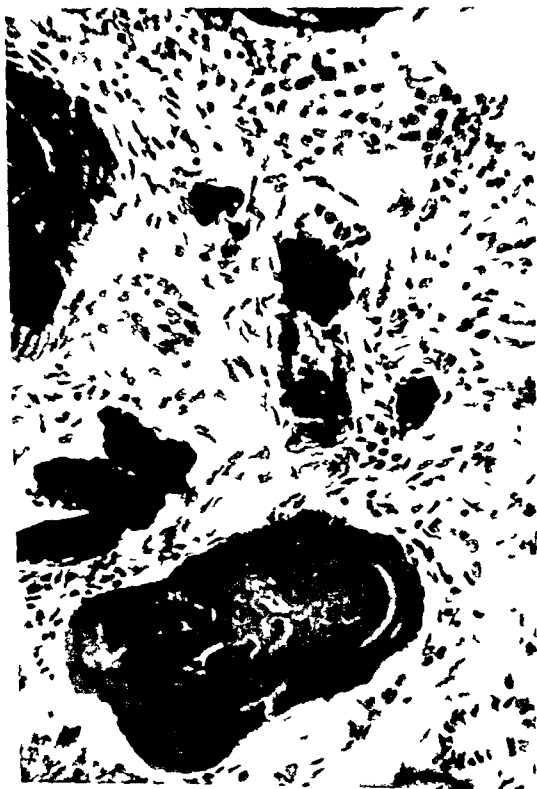


Figure 2 Photomicrograph of section of kidney showing tubular atrophy and calcification. ( $\times 260$ )



larged weighing 12 grams together Histologic study revealed only moderate lipid depletion with no evident hyperplasia A terminal bronchopneumonia was present

The cause of death was hypokalemia with the associated cardiac functional impairment The anatomic defect in the kidneys seems best designated as a pyelonephritis The cause of the hypokalemia at first glance seems related to the renal pathology with the condition being such as to constitute an example of potassium-losing nephritis Such cases have been reported recently and especially in the British literature However renal loss of potassium of such magnitude as to result in the low potassium syndrome is considered quite rare Unfortunately urinary potassium studies were not performed The renal conditions in which a low serum potassium have been encountered not infrequently are the Fanconi syndrome and the Albright Lightwood syndrome However these conditions can be readily excluded in that the latter situation generally shows a hyperchloremia and in the case of the Fanconi syndrome the clinical and laboratory findings are characteristic It is possible that some of the reported cases of potassium losing nephritis may actually represent primary aldosteronism This seems excluded in this instance on the basis of lack of inciting adrenal pathology It should be emphasized that potassium depletion in itself may give rise to renal dysfunction A specific lesion not infrequently can be demonstrated either on biopsy or at autopsy in instances of hypokalemia In this condition extensive hydropic changes may be seen within the renal tubules Although the possibility of a true potassium losing nephritis cannot be excluded in this case the history given by the patient of excessive laxative ingestion raises the possibility that rather than a renal loss of potassium loss may have resulted from a chronic diarrhea secondary to the stated laxative ingestion This would explain the hypokalemic episode six years previously The reported cases have not shown the severe renal functional impairment as noted in this case however It is quite possible that in this case some renal dysfunction was due to a potassium loss in the stool which together with the pre-existing renal disease may have resulted in the progressive renal impairment noted

#### Pathologic diagnoses

- 1 Hypokalemia from renal and enteric potassium depletion
- 2 Chronic pyelonephritis

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## SERVICE ARTICLE

# STREPTOCOCCAL PROPHYLAXIS IN NAVY RECRUITS WITH ORAL AND BENZATHINE PENICILLIN

PAUL F. FRANK, M.D.

**E**XPERIENCE with penicillin prophylaxis against streptococcal infections has shown that the administration of 157 mg (250,000 units) of buffered oral penicillin G twice daily for a period of 10 days is effective in disrupting streptococcal epidemics among recruit populations.<sup>1</sup> Recently, however, a severe streptococcal epidemic that occurred at this training center required two such courses of penicillin before it was brought under control.<sup>2-4</sup> There were two basic reasons for this: (1) The initial course of penicillin was not sufficient to eradicate the carriage of the epidemic strain in such a heavily infected population, and (2) there were enough individuals who did not receive penicillin prophylaxis, either because of hypersensitivity to penicillin or for administrative reasons, to act as a reservoir for reseeding the population.

Since the use of long acting benzathine penicillin was proved to be effective in the control of streptococcal infections among rheumatic fever patients,<sup>5</sup> its prophylactic application among military personnel has been given a limited trial.<sup>6-7</sup> In an early investigation in a military population, however, a rather high incidence of hypersensitivity reactions was encountered,<sup>6</sup> and mass prophylaxis in recruit populations has not been attempted until recently.

The present investigation was undertaken for two reasons. First, an adenovirus vaccination study was being conducted in the recruit population at this naval station, and some form of penicillin prophylaxis was mandatory to control streptococcal disease in order that a valid evaluation of the vaccine program could be made. Second, a limited amount of benzathine penicillin was available for trial, and it was desirable to control streptococcal carriage among new men arriving for training. This was necessary during and for a period subsequent to an oral peni-

cillin prophylactic program among onboard recruits, to prevent any recurrence of a streptococcal epidemic at the conclusion of oral penicillin prophylaxis

This report includes observations on streptococcal prevalence before during and subsequent to the institution of penicillin prophylaxis on the distribution of the two different penicillin preparations among the recruit population and the proportion of recruits under effective prophylaxis at any one time during the study on the incidence of isolation of beta hemolytic streptococci among men receiving either penicillin preparation during the various periods of the study, and the time when men previously protected with benzathine penicillin acquired group A streptococci and on the incidence and severity of hypersensitivity reactions resulting from the use of the oral or benzathine penicillin preparations

## MATERIALS AND METHODS

### Penicillin Prophylactic Program

Penicillin prophylaxis consisted of two different types of penicillin administered by two different routes From 18 January to 27 April 1956 all recruits reporting aboard this training center who denied allergy to penicillin were given a single intramuscular injection of 495 mg (600 000 units) of benzathine penicillin in the buttocks within four to five days after arrival The penicillin was given at the time of adenovirus vaccination and the first series of routine immunizations

Recruits already in training who did not claim hypersensitivity to penicillin including those in preparatory school detention and reassignment companies brig and medical and dental holding companies received for a 10-day period beginning 23 January 157 mg (250 000 units) of buffered oral penicillin G twice daily (before breakfast and before the evening meal) For an additional 30-day period ending 3 March or until termination of training whichever occurred first the dose was reduced to once daily All penicillin tablets were distributed by the Medical Department under the supervision of the Senior Medical Officer to the training regiments where the tablets were issued to the company commanders for administration to the recruits Any recruit claiming a history of hives or allergy to penicillin was required to report to one of the field dispensaries where he was examined by a medical officer and excused from the program if the claim was substantiated

### Collection of Material To Be Used in the Evaluation

*Bacteriological cultures* Throat cultures for the isolation of beta hemolytic streptococci were collected from recruits examined in the barracks during weekly surveys for the incidence of re-

spiratory illnesses. Companies representative of each week of training were chosen at random so that approximately one fifteenth of the training regiment was sampled weekly. In addition, daily throat cultures were taken on recruits reporting to sick bay with febrile respiratory illnesses. The cultures were seeded on sheep-blood agar plates and examined for the presence of beta hemolytic streptococci. All streptococcal strains isolated were identified serologically as previously described.<sup>8</sup>

**Penicillin reactions** During the period of penicillin prophylaxis, any recruit presenting himself to the regimental infirmary with symptoms of penicillin hypersensitivity was examined by a medical officer. He completed a questionnaire on all reactions seen, recording the type of penicillin given, the interval between injection and appearance of symptoms, the symptoms encountered, and the relative severity of the reaction.

**Rheumatic fever** Only confirmed cases of rheumatic fever among recruits in training were tabulated in this study.

## RESULTS

Prior to the beginning of penicillin prophylaxis, the respiratory disease admission rates rose from 8 per 1 000 per week on 3 December to 15 per 1 000 per week on 31 December and returned to about 7 per 1,000 per week around 14 January (fig. 1). The isolation of group A streptococci from recruits with respiratory

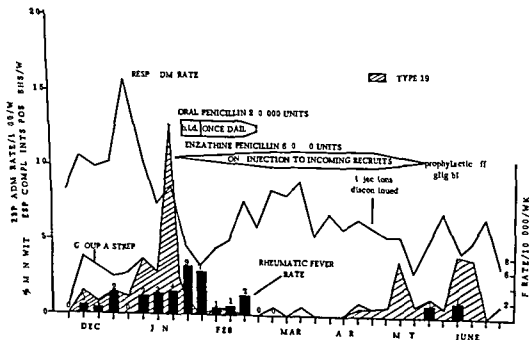


Figure 1 Incidence of streptococcus isolation, rheumatic fever and hospital admissions for acute respiratory diseases during oral penicillin or benzathine penicillin prophylaxis winter of 1955-1956 Great Lakes III

disease complaints seen in the barracks did not exceed 4 per cent. However during this time large mucococcus strains of type 19 streptococci were being recovered. During the second week in January both respiratory disease admission rates and streptococcal isolation rates began to climb, the latter at a greater rate. At this time four cases of rheumatic fever were reported at the hospital. On the strength of the increase in streptococcal isolations, the occurrence of rheumatic fever, and the prevalence of a single type of streptococci that exhibited mucococcus colonies on blood agar plates so characteristic of epidemic streptococci, penicillin prophylaxis was instituted on 18 January.

During the period of prophylaxis, respiratory disease admission rates ranged between a low of 3 per 1 000 per week in early February to a high of 9 per 1 000 per week in the third week of March. Group A streptococcal isolations during this period were negligible and only toward the end of the prophylactic period did the streptococcal isolation rates begin to increase, fluctuating between 1 and 4 per cent through May and June. Most of these isolations were type 19.

The prevalence of beta hemolytic streptococci in the recruit population prior to penicillin prophylaxis is reflected not only in the sharp rise in streptococcal isolation rates, but also in the high incidence of rheumatic fever (20 cases) occurring in the five week period following the beginning of prophylaxis (fig 1). In addition, in the two weeks just prior to prophylaxis, six cases of scarlet fever were reported among the recruits. Similarly, the evidence of a small outbreak of streptococcal infections in the last week of April and first week of May was evident in the appearance of two additional cases of rheumatic fever and two cases of scarlet fever.

In any penicillin prophylactic program there will be a few individuals who will not be able to participate in the program because of hypersensitivity to penicillin. In addition, there will be others who will not receive prophylaxis for administrative reasons or who will not be under effective prophylaxis due to the expiration of the prophylactic action of the penicillin preparation under investigation. Figure 2 shows the percentage of recruits under effective penicillin prophylaxis at any one time during the study period. Early in the program, about 15 per cent were not given any penicillin. These men had less than 10 days of training left and would not have received the full 10 days of oral prophylaxis. Subsequently, for a period of about three weeks, approximately 98 per cent of the recruits were under effective penicillin prophylaxis. During the month of February, the proportion of men receiving the oral preparation declined from 85 to 35 per cent, while those men under effective benzathine penicillin (21 days or less) increased to 42 per cent. During this



TABLE 1 I l t o f b i a h m l y t c s t p t c c f m N y t  
t g r l p n l l G b z a t h p c l l i t h p r i d 23  
J a r y t h r o g b 3 M b 1956

	C m p a n s c i l l i n g		C m p a n s c e i g	
	N m b	P e t	N u m b	P e r t
	M x c l d d f m p p h y l			
Pen l l i s i t i	44	2 2	45	4 5
N m b p t	5	11 4	2	4 5
N u m b e g p A	3	6 8	0	0
M l l a n			136	13 6
N u m b p t i			9	5 9
N u m b r g r p A			0	0
S b t t l	44	2 2	181	18 1
	M e n r i g p p h y l a x			
N u m b c l t u r e d	1981	97 8	817	81 9
N u m b r p o t i v	47	2 4	11	1 3
N u m b r g p A	8	0 4	1	0 1
T t l c l t u r d	2025		998	

Typ 19

S f t h w r t y p 19

Typ 5 l d g d y f g b h p l l

streptococcal positive throat cultures was about the same among men receiving either penicillin preparation, group A strains of the epidemic type were found only among companies receiving oral penicillin where a rate as high as 6.8 per cent of uninoculated men carried this type. The single isolation of a group A strain among the benzathine penicillin treated companies occurred in a recruit who had received his injection 8 days before; however this strain proved to be type 5. Many of the non group A strains isolated during this period among penicillin treated men were minute group G. One additional fact deserving attention is that approximately 18 per cent of the men in the benzathine penicillin treated companies did not receive prophylaxis during the period of combined oral and benzathine prophylaxis.

Data on the results of the second period of study when only benzathine penicillin was given to the recruits arriving for training are shown in table 2. Cultures for the isolation of beta hemolytic streptococci were obtained from 4,203 men, only 2.8 per cent of whom claimed penicillin hypersensitivity. An addition

al 6 6 per cent were excused from prophylaxis for administrative reasons. The total percentage of men not receiving prophylaxis during this period was approximately one half that in the previous study period.

TABLE 2 Isolation of beta hemolytic streptococci from Navy recruits among companies receiving benzathine penicillin in the period 4 March through 27 April 1956

	Cultured		Positive		With group A streptococci	
	Number	Per cent	Number	Per cent	Number	Per cent
	Receiving benzathine penicillin					
Penicillin sensitive	119	2 8	5	4 2	1	0 8
Other	279	6 6	5	1 2	2	0 7
Subtotal	398	9 4	10	2 5	3	0 8
	Receiving benzathine penicillin					
	3805	90 6	87	2 3	6	0 2
Total	4203	100	97	2 3	9	0 2

Type 19 isolations

For type 19 and two types isolations All isolations  
29 days or more after receiving benzathine penicillin

Although the recovery of beta hemolytic streptococci among men receiving penicillin prophylaxis was the same as among those not receiving prophylaxis, there were significantly fewer isolations of group A strains in the treated recruits. Actually, all the group A strain isolations from the treated men occurred 29 days or more after receiving benzathine penicillin prophylaxis. Type 19 strains were being isolated from the treated as well as the untreated recruits during this period of the study.

Following the administration of benzathine penicillin prophylaxis, an additional two-month period of observation was undertaken. The streptococcal isolation rates are shown in table 3. During this period, about one third of the recruits came from companies that had received benzathine penicillin prophylaxis upon arrival at this station. As can be seen, group A type 19 isolations were approximately the same among recruits from treated and untreated companies.

One of the basic issues in any penicillin prophylactic program, particularly in the case of a depot type penicillin, is the experience of the treated companies during the period when the



protection of the penicillin has been exhausted. To shed some light on this question cultural data from companies in their first four weeks of training were compared with that of companies in their fifth through ninth week of training for each of the three study periods. It was assumed that the protective effect of penicillin was minimal after 4 weeks. During each of the study periods a comparison was made between those men receiving or not receiving prophylaxis (table 4).

TABLE 3 Isolation of streptococci from Navy recruits during the period of first 4 weeks of training and from 5th through 9th week of training, 1956

	Benzathine penicillin treated men			Untreated men
	Treated	Untreated		
		Penicillin	Other	
Number of positive cultures	70	0	2	94
Percentage	53	0	13.4	42
Group A				
Number	21	0	1	24
Percentage	16	0	6.7	11
Number of isolates	1333	15	15	2267

Typ 19

In the period of oral prophylaxis there were no significant differences in group A isolation rates between the early and late training periods from recruits receiving or not receiving benzathine penicillin. It should be remembered that during this period 80 to 95 per cent of the recruits were under effective prophylaxis. Similarly there was no apparent increase in group A acquisitions among treated men in the later periods of training when only benzathine prophylaxis was given. However recruits in the benzathine treated companies who did not receive the antibiotic did exhibit an increase in streptococcal acquisitions in the fifth to ninth week of training. During this period only 23 to 35 per cent of the recruits were under effective penicillin prophylaxis.

In the four weeks following discontinuance of benzathine penicillin prophylaxis of arriving recruits, from 2 to 15 per cent of the recruit population was under effective treatment. As can be seen the effect of benzathine penicillin is manifested only in the first four weeks of training. Streptococcal acquisitions became significantly increased in the latter half of training in both treated and untreated men.

TABLE 4 Comparison by period of the frequency of isolation of group A streptococci from recruits receiving benzathine penicillin prophylaxis and from untreated recruits

	Weekly frequency					
	Frequency			Frequency		
	Cultured	Group A	Isolated	Cultured	Group A	Isolated
	No.	No.	Percent	No.	No.	Percent
	Period of benzathine penicillin prophylaxis					
Recruits	776	1	0.1	41	0	0
Untreated	166	0	0	15	0	0
	Period of benzathine penicillin prophylaxis					
	Period of benzathine penicillin prophylaxis					
	Period of benzathine penicillin prophylaxis					
	Period of benzathine penicillin prophylaxis					
	Period of benzathine penicillin prophylaxis					
During benzathine prophylaxis	1911	3	0.2	1894	3	0.2
Treated	129	0	0	269	3	1.1
Untreated						
Period of benzathine prophylaxis	254	1	0.4	10.9	20	2.0
Treated	1499	11	0.7	768	13	1.7
Untreated						

Typical group A streptococci isolated from recruits

In connection with an adenovirus vaccine study conducted concurrently with the penicillin prophylactic program, cultures from 1,688 recruits coming to the sick bay with febrile respiratory disease complaints were examined for the presence of beta hemolytic streptococci during the period of 17 March through 12 May. During the period of benzathine penicillin prophylaxis, an average of 3.6 per cent of the recruits from whom cultures were obtained exhibited positive culture for group A beta hemolytic streptococci (table 5) and all but two of the strains proved to be type 19. This would indicate that up to 3.6 per cent of the men reporting to the dispensary with febrile respiratory illnesses possibly were suffering from streptococcal infections. However, about one fifth of the 61 men with positive cultures did not receive prophylaxis.

#### Acquisition of Group A Streptococci by Benzathine Treated or Untreated Recruits

An important factor in the effectiveness of the penicillin prophylactic program in addition to the eradication of the beta hemolytic streptococcus from the nose and throat, is the period an individual is protected against the acquisition of streptococci. During this study there were available isolations of group A streptococci from recruits receiving the single injection of 495 mg (600,000 units) of benzathine penicillin and isolations from those not receiving prophylaxis. The distribution of these isolations in days after injection or days aboard, respectively, is depicted

protection of the penicillin has been exhausted. To shed some light on this question, cultural data from companies in their first four weeks of training were compared with that of companies in their fifth through ninth week of training for each of the three study periods. It was assumed that the protective effect of penicillin was minimal after 4 weeks. During each of the study periods, a comparison was made between those men receiving or not receiving prophylaxis (table 4).

TABLE 3. *Isolation of streptococci from Navy recruits during the first four weeks of training and the fifth through ninth week of training, 28 April through 30 June 1956.*

	Benzathine penicillin treated group			Untreated group
	Treated	Untreated		
		Penicillin	Other	
Number positive	70	0	2	94
Percentage	53	0	13.4	42
Group A				
Number	21	0	1	24
Percentage	16	0	6.7	11
Number cultured	1333	15	15	2267

Typ 19

In the period of oral prophylaxis there were no significant differences in group A isolation rates between the early and late training periods from recruits receiving or not receiving benzathine penicillin. It should be remembered that during this period 80 to 95 per cent of the recruits were under effective prophylaxis. Similarly, there was no apparent increase in group A acquisitions among treated men in the later periods of training when only benzathine prophylaxis was given. However, recruits in the benzathine treated companies who did not receive the antibiotic did exhibit an increase in streptococcal acquisitions in the fifth to ninth week of training. During this period, only 23 to 35 per cent of the recruits were under effective penicillin prophylaxis.

In the four weeks following discontinuance of benzathine penicillin prophylaxis of arriving recruits, from 2 to 15 per cent of the recruit population was under effective treatment. As can be seen, the effect of benzathine penicillin is manifested only in the first four weeks of training. Streptococcal acquisitions became significantly increased in the latter half of training in both treated and untreated men.

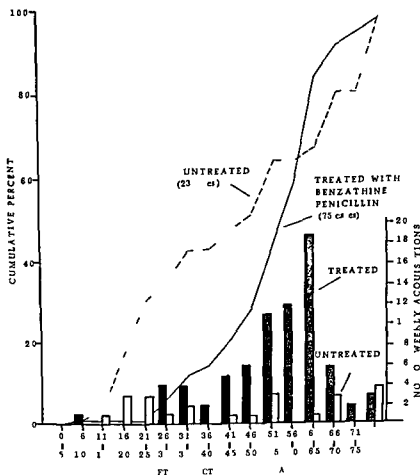


Figure 3 Time of acquisition of Group A streptococci by those recruits treated or untreated with benzathine penicillin winter of 1955-1956

that reactions to benzathine penicillin were more severe than from the oral preparation (table 6). In addition, approximately 86 per cent of those who reacted to oral penicillin G and 60 per cent of those reacting to benzathine penicillin responded to outpatient therapy. The only other side effect experienced by the recruit was severe local pain at the site of injection for a period ranging from 1 to 3 days. No sterile abscesses were encountered.

Figure 4 shows the relationship of time of injection of benzathine penicillin or starting of oral prophylaxis until the manifestation of symptoms of hypersensitivity. The number of cases of hypersensitivity among men receiving the oral preparation occurred at a uniform rate during the first 20 days of prophylaxis, during which time 80 per cent of the reactions had taken place. An occasional reaction was observed as long as the 40th day following the beginning of prophylaxis. Reactions of men treated with benzathine penicillin occurred most frequently between the 8th and the 14th day following injection. About two thirds of the cases reported to sick bay during this period. Only a few reactions were observed beyond the 15th day, two occurring 51 and 52 days,

respectively following inoculation. A search of the medical records of these two men failed to indicate that any additional penicillin had been received.

TABLE 6. Penicillin prophylaxis in the Navy recruit population.

	Oral		Benzathine	
	Number	Percentage	Number	Percentage
Men with streptococcal prophylaxis	65 12,707	0.51	129 13,549	1.1
	Residence			
Uncolored	51	83.7	114	93.5
Anglo-American	4	6.6	21	17.2
Joint population	8	13.1	34	27.9
Total	61		122	
	Sensitivity			
Clinical impression				
Mild	39	66.2	52	42.6
Moderate	19	32.4	64	52.5
Severe	1	1.7	6	4.9
Total clinical	59		122	
Hospitalized	9	13.8	53	41.4
Hospitalized (fatalities)	9	0.07	53	0.39

Source: Data from the United States Armed Forces Medical Journal, Vol. 1, No. 4, 1955, pp. 1-10.

## DISCUSSION

From the overall picture depicted in figure 1 it appears that the prophylactic use of oral penicillin G and benzathine penicillin was effective not only in disrupting a streptococcal disease outbreak among the recruit population but also in keeping the isolation rate of group A beta hemolytic streptococci at a minimum during the winter of 1955 and 1956. On the other hand, in spite of the rather intensive penicillin prophylactic program, there appeared to have been a recrudescence of the outbreak during April, May, and June just before benzathine prophylaxis was discontinued.

tured The same type of streptococci was isolated during this period and two cases each of rheumatic fever and scarlet fever appeared, suggesting that this strain was similar to or the same as that isolated earlier in the year, and that eradication of the source of epidemic streptococci was not accomplished

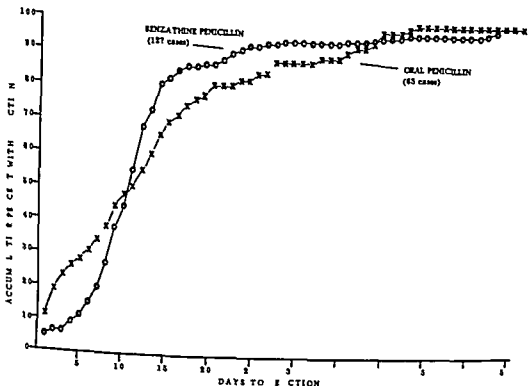


Figure 4 Days to onset of symptoms of penicillin hypersensitivity reaction in recruits receiving oral or benzathine penicillin.

This reappearance of the outbreak could have resulted from (1) carriage of the epidemic strain among individuals not receiving penicillin prophylaxis, who acted as a nucleus for the spread of streptococci when prophylaxis was terminated (2) unsuccessful eradication of the epidemic strain among men receiving treatment, who also were a source of epidemic streptococci in the post prophylactic period and (3) perpetuation of the strain among benzathine penicillin treated men who acquired, in their later weeks of training when the protective antibiotic levels in the blood had been dissipated, epidemic streptococci from untreated or treated recruits carrying the strain

It was seen that in both the oral penicillin and benzathine-treated companies there was a proportion of the men who did not receive penicillin prophylaxis, reaching as high as 18 per cent in the benzathine treated companies. Although isolations of group A streptococci were not excessive in these men, the presence of type 19 streptococci may ultimately have been responsible for the subsequent streptococcal outbreak.

The family history was noncontributory. Both the mother and father were living and well and there were no siblings.

On physical examination the abdomen appeared abnormally large and on the right side a firm mass extended from the costal cage to the pelvic brim and medially to the midline. Other physical examination findings fitted a normal pattern for age.

Cystoscopy revealed no pathologic condition but a retrograde pyelogram showed a greatly enlarged right kidney with the ureter extending across the midline (fig 1). There was marked distortion of the calyces with the superior calyces depressed inferolaterally and



Fig 1 Retrograde pyelogram shows greatly enlarged right kidney with ureter extending across the midline and distal part of abdomen

the inferior calyces pushed to the left and upward. The calyces and pelvis of the left kidney were within normal limits. Roentgenograms of the skeletal system and chest were negative as were urinalysis and hematologic studies.

The urologic and surgical consultants were in agreement with the admission diagnosis of Wilms's tumor and it was decided to perform

a nephrectomy to be preceded and followed by x ray therapy. The patient had six days of preoperative x ray treatment totaling 1200 r in air the daily therapy regimen being 200 kvp 20 ma 10 mm Al 0.5 mm Cu 50 cm dist 10 x 15 200 r 6 2" alternating the anterior and posterior right abdominal fields. At operation on 31 October the mass was roughly one half the original size. The kidney and tumor were removed through a transperitoneal approach. The pathologic diagnosis of the specimen which has been corroborated by several pathologists was Wilms tumor of the right kidney showing radiation necrosis (fig. 2).

The patient was given a nine day postoperative course of x ray therapy totaling 1800 r in air using the same radiation factors as in the preoperative course. Following the operation she had an uneventful stay in the hospital aside from a few mild bouts of radiation sickness and was discharged home on 19 December.

From 19 December 1950 to March of 1953 the patient had frequent follow up investigations for metastasis or recurrence. She enjoyed excellent health and progressed in a normal growth and development pattern with no signs or symptoms relating to the previous pathologic condition in her right kidney.

#### Second Hospitalization

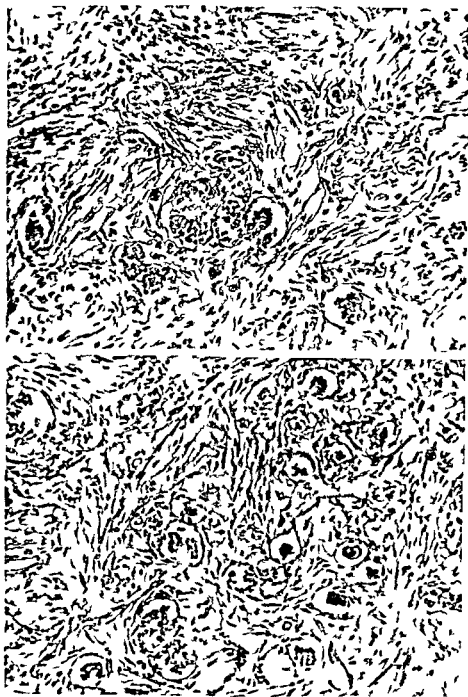
On 23 March 1953 the patient was admitted to the U. S. Naval Hospital Great Lakes Ill because of a mass in the left side of the abdomen. Two days previously she had complained of pain in the left flank and her mother discovered a mass there. There had been no premonitory symptoms although two and one half weeks prior to admission the patient had been examined for a febrile illness by a doctor who said that he felt nothing in the abdomen.

Physical examination revealed a well developed healthy appearing girl with no evidence of weight loss. There was a right upper quadrant scar and an easily palpable mass that filled the left side of the abdomen from the rib cage to the iliac crest and medially to the umbilicus. There were no other physical findings of note.

The hemoglobin was 11.0 grams per 100 ml the red blood cell count 3,760,000 per  $\mu$ l the white blood cell count 10,950 per  $\mu$ l and the blood urea nitrogen 13.5 mg per 100 ml. Examination of the urine revealed rare white and red blood cells but no albumin.

An intravenous pyelogram on 24 March (fig. 3) showed a fairly normal calyceal pattern in the left kidney. There was a mild hydro-nephrosis with upper ureteral dilatation and displacement medially. A large mass which could be nodes tumor in the lower pole or simply





*F g 2 Phot m cr g ph of t s f m ght k dn y w th W lm t m  
b w g ad t c*



*Fig 3 Intravenous pyelogram showing medial displacement of ureter and mild hydronephrosis caused by large mass in area of lower pole of left kidney*

a hydronephrosis in the lower segment of a reduplicated kidney was present retroperitoneally causing bowel and ureteral displacement. The kidney and related mass were freely mobile. Other x-ray and laboratory procedures were noncontributory. They presented no evidence of metastasis.

The most likely possibility appeared to be a tumor in the lower most portion of the one remaining kidney and it was decided to irradiate the tumor mass lightly to reduce its size then remove it and irradiate to a moderate extent postoperatively. Preoperatively the patient was given a total of 830 r in air equally divided between left anterior and posterior midabdomen from a 220 kvp 15 ma machine with tube distance of 50 mm and filtration of 0.5 mm of copper and 1.0 mm of aluminum. With this therapy the blood pressure, blood count and blood urea nitrogen remained normal.

At operation on 4 April the tumor had shrunk to the size of a lemon and was slightly cystic and friable. The operative report stated that

approximately the lower one third of the kidney was represented by a soft gelatinous multicolored multinodular tumor mass with hemorrhagic necrotic zones and a very thin intact veil like capsule that was attached by thin adhesions to the surrounding tissues. When the adhesions were divided and the entire tumor mobilized two small aberrant arteries and veins were seen to enter the lower pole of the kidney directly into the tumor mass. These were doubly ligated and divided.

The upper two thirds to three fourths of the kidney appeared normal in size shape color and consistency and a fairly sharp line of demarcation was present where this portion of the kidney merged with the tumor. A soft shod rubber clamp was applied to the renal pedicle with just enough pressure to control bleeding after which the kidney was resected. The incision extended circumferentially in a line about 1.7 cm proximal to the tumor demarcation in a normal appearing portion of renal parenchyma and transected the lowest minor calyx which was closed with 0000 chromic catgut around a calyostomy tube size 14 F. Irrigation of this tube with sterile saline solution showed a crystal clear return flow. Several interlobar and arcuate arteries were identified by loosening the renal pedicle clamp. These were ligated. The renal parenchyma was then approximated with a thin layer of fat (for hemostasis) between and was mattress sutured using plugs of perirenal fat to prevent the sutures from cutting into renal cortex. A second row of interrupted sutures were placed to effectively close the anterior and posterior parenchyma. The renal pedicle clamp was now removed and no bleeding was observed. One Penrose drain was placed in the depths of the wound and along with the calyostomy tube was brought out through the posterior angle of the wound and secured. No surgical shock was evident at any time and the anesthesia was perfect.

The gross specimen sent for diagnosis consisted of a portion of kidney with attached tumor which was well circumscribed grayish brown and about 4 cm in diameter. The portion of kidney was 1.5 by 3.0 by 3.5 cm. Microscopically (fig 4) the tumor had a myxomatous occasionally fibrosarcomatous stroma containing islands of deeply staining basophilic spindle shaped nuclei or tubular structures lined by low cuboidal epithelium with hyperchromatic nuclei. There were occasional foci of hemorrhage and necrosis. The tumor had invaded the margins of the renal parenchymal tissue and in the medullary region had obstructed collecting ducts causing dilatation. There were some acute inflammatory cells within the stroma of the tumor. The diagnosis as confirmed by several pathologists was Wilms tumor.

Postoperatively the patient did very well. Her blood pressure rose to 138/90 mm Hg on the second day after operation but had returned to normal two days later. Blood chemistry determinations were remarkably normal. The blood urea nitrogen was 4.5 mg per 100 ml.

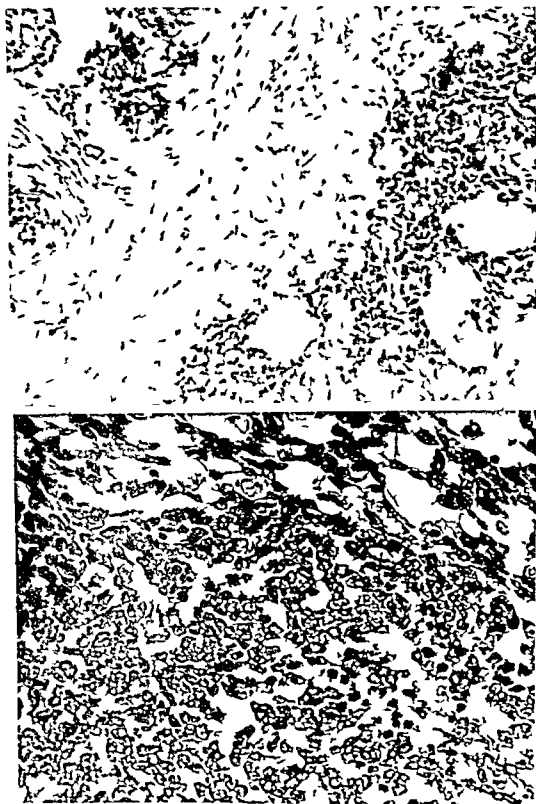


Figure 4 Photomicrographs of sections of specimen removed from left kidney showing Wilms tumor and areas of necrosis. ( $\times 430$ )

four hours after operation and reached 17.5 six days later but had returned to 9.5 the day prior to discharge. Creatinine, chlo-ride, hemoglobin and red blood cell count remained essentially normal throughout. The 24 hour postoperative fluid intake was 1280 ml (intravenous) and urinary output was 820 ml. The specific gravity of the urine varied during the first nine days from 1.010 to 1.020.

The patient was given a course of postoperative x-ray therapy using the same radiation factors and regimen as for the preoperative course but totaling only 440 r in air.

The indwelling catheter was removed on the fourth postoperative day and the calyostomy tube on the eleventh day. The remainder of the hospital stay was without incident and the patient was discharged on 16 April.

From 16 April 1953 to the present the patient has been followed closely. All results of repeated examinations and laboratory studies have been within normal limits or promptly returned to normal. Four years after the second operation a checkup at Tripler U S Army Hospital, Honolulu, Hawaii, made by Captain L. Luke, MC USA, showed blood urea nitrogen of 13.4 mg per 100 ml, a normal left excretory urogram with absence of the right kidney (fig. 5) and a normal

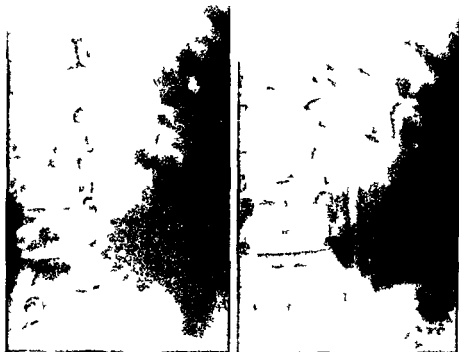


Fig. 5. Excretory urogram of left kidney left after 5 months post operation. Right kidney absent.

roentgenogram of the chest and long bones. The patient was completely asymptomatic and leading an active normal life. A complete physical examination at the same hospital in November 1957 revealed that her condition had continued unchanged with no evidence of metastasis or recurrence of the tumor. This was confirmed by report of 13 March 1958.

### DISCUSSION

Embryonic mixed tumors were well evaluated as long ago as 1897 by Waller,<sup>1</sup> who pointed out that with early treatment there was at least some hope of survival. One question he raised still is not answered namely whether bilateral tumors are separate in origin or have a metastatic relationship.

In the present case malignancy of the right kidney was treated by nephrectomy at 14 months of age. This is approximately the age at which Gross and Neuhäuser<sup>2</sup> consider the best results are obtained. The patient showed no evidence of metastasis or recurrence for 20 months, then a tumor was discovered in the remaining left kidney. This was treated by resection, which Campbell recommended in such a situation even though he considered that it offered only "an exceedingly long chance" of survival.

The passage of five years following the resection without any evidence of metastasis or recurrence makes it seem improbable that either will occur. Puschke reported two cases of full term uneventful pregnancy several years after treatment for unilateral Wilms tumor. This patient who has only part of one kidney has shown normal growth and development presumably because of compensatory hypertrophy of the remaining portion of kidney as described by Addison.<sup>3</sup> In her case although an entirely new tumor could at some time arise from the remaining kidney tissue such an untoward outcome appears to be unlikely.

### SUMMARY

The possibility of survival after surgical removal of bilateral Wilms tumor accompanied by appropriate preoperative and postoperative deep x-ray therapy is illustrated by report of a case. Seven and one half years after removal of the right kidney and five years after resection of the left the patient continues in good health with no evidence of metastasis or recurrence. In spite of removal of two thirds of her normal kidney mass her pattern of growth and development apparently is unaltered.

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### TEAMWORK IN WRITING

Anyone developing new procedures or having new concepts should be willing to discuss and share them with others. No one should underestimate the power of an idea or the effectiveness of the pen. A discussion may be concerned with clinical or experimental subjects. For example, before a disease can be discussed, the normal findings should be given or shown, thus laying the basis for an understanding of the altered physiologic state. Anyone writing should recognize that research is the result of cooperation and team work. An ophthalmologist may need the assistance of the clinician, the histochemist, the physiologist, the pathologist and other specialists in medicine to aid him in his research. These work as a team, thus each may be better informed to the end that the patient may be better served. There are compensations from such united efforts as (1) offering the opportunity for men in various specialties to better know each other and understand the language of their respective field of interest, (2) through the publications of the results of the work, wider dissemination of the findings of research will be made possible. The writer must recognize that the subject may not only be of interest to those in his specialty but may stimulate the interest of those in related medical fields. His contribution is but a part of a larger sphere of scientific endeavor in which many may participate. This may be an ideal, but in actuality, often the most valuable findings have stemmed from the work of one individual who with a dynamic idea had a practical, workable plan of procedure in solving a problem.

—EDITORIAL

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# Thyrotoxicosis With Thyrocardiac Crisis and Granulocytopenia

## Following Therapy With Propylthiouracil

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VICTOR F CORSIGLIA Jr *Lieutenant MC USNR*

THE TERM "thyrotoxic crisis" is now generally used to imply a fulminating increase in all signs and symptoms of thyrotoxicosis. Such a crisis is a dire medical emergency that is life endangering. McArthur and associates<sup>1</sup> considered thyroid crisis not a complication of thyrotoxicosis but an intrinsic feature of the disease—a state being reached in which the patient is no longer capable of adjusting to the strain imposed by the hyperthyroidism. It is a multifaceted syndrome and the symptomatology that develops depends on the relative vulnerability of body systems such as the central nervous system, the cardiorespiratory system, the gastrointestinal tract, and the hepatorenal or the adrenal-pituitary axis.

We have observed a patient with thyrotoxic crisis who was gravely ill and survived the critical period with therapy directed mainly at improving cardiorespiratory function. This case is best described as one of thyrocardiac crisis.

### CASE REPORT

A 38 year old Caucasian married woman was first seen in the emergency outpatient clinic of this hospital on 3 September 1956 complaining of tachycardia, palpitation, and irregularity of her heart beat. Examination revealed a completely irregular rhythm with a ventricular rate of 130 per minute. Her blood pressure was 170/80 mm Hg and her thyroid gland was diffusely enlarged. An electrocardiogram demonstrated intermittent auricular fibrillation with a ventricular response of 170 per minute alternating with sinus tachycardia at a rate of 140 per minute. The auricular fibrillation spontaneously subsided and the patient felt well. Protein bound iodine was 20.5  $\mu$ g per 100 ml. The patient failed to keep her appointment for evaluation in the medical clinic.

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From U S N 1 H p t l Camp Pendler Calif. C mdr Morg n s now assigned to N v l m d c l R s at h Unit No 2 APO 63 S a Franc sc Calif.



On 14 February 1957 the patient again appeared at the emergency outpatient clinic and was admitted to the hospital. She stated that since September 1956 she had had short episodes of palpitation with a rapid irregular heart beat and that during the three days prior to her admission this condition had been continuous. She had noted moderate dyspnea and orthopnea. For the preceding 24 hours there had been nausea but no vomiting. She was employed as a school teacher and had worked the day of admission. She had noted nervousness, a gradual onset of difficulty in sleeping, increased appetite, and a decreased tolerance to heat. She perspired easily. There had been no weight loss but rather a gradual 4 pound gain during the past month. Menstrual periods were regular every 28 days but scanty in flow and lasting one to two days.

She had lived most of her life in Wisconsin. Seventeen years prior to admission she had a thyroglossal duct cyst excised without complications. She also had an appendectomy in 1954 and pneumonia at ages 8 and 16 years. She had one child, 12 years of age.

**Physical Examination.** The patient was well developed and well nourished but was moderately nervous and apprehensive. Her temperature was 99.6° F and respirations were 22 per minute. Her skin was warm and moist. Slight bilateral exophthalmos was present without other eye signs. A coarse tremor was noted. The thyroid gland was diffusely enlarged approximately three times normal size with a small well healed surgical scar over the cricoid area. The heart beat was irregular with a ventricular rate of 140 per minute. There was a systolic murmur over the apical area. Blood pressure was 180/90 mm Hg. A few moist rales were present in the lung bases. The liver and spleen were not palpable and there was no significant adenopathy.

**Laboratory Studies.** The white blood cell count was 7,500 per  $\mu$ l with 55 per cent neutrophils, 40 per cent lymphocytes, and 5 per cent monocytes. Hemoglobin and hematocrit were normal. Urinalysis was negative. The serologic test for syphilis was negative. Total serum cholesterol was 130 mg per 100 ml, protein-bound iodine was 12.8  $\mu$ g per 100 ml, and the basal metabolic rate was plus 60 per cent. An electrocardiogram on 14 February demonstrated auricular fibrillation (fig. 1). A roentgenogram of the chest on 15 February showed edema of the lower lung fields (fig. 2).

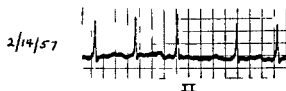


Fig. 1. Atrial fibrillation. 14 February 1957.



*Figure 2 Edema of both lower lung fields shown in roentgenogram made on 15 February 1957*

**Course in Hospital** On admission therapy consisted of bed rest sedation with Nembutal a high caloric diet and 200 mg of propylthiouracil every eight hours Starting four hours after the first propylthiouracil was administered 0.6 ml of a saturated solution of potassium iodide was given orally three times daily

During the first 24 hours of hospitalization the patient appeared to be doing well on this regimen having no respiratory difficulty eating well and not appearing to be particularly nervous or toxic During the second night she became restless and apprehensive and could not sleep These were interpreted as toxic symptoms and she was sedated heavily with barbiturates and morphine sulfate with some diminution of symptoms

Early the next morning the patient became acutely dyspneic orthopneic cyanotic and semicomatose with thrashing movements of the extremities Moist rales were present throughout both lung fields The heart beat was totally irregular at 150 per minute and the heart sounds were faint Blood pressure was 140/90 mm Hg and temperature

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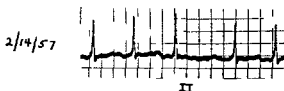


Fig. 1 Atrial fibrillation evidenced by ECG made on 14 February 1957.

The propylthiouracil was discontinued and 1 200 000 units prophylactic procaine penicillin daily and 2 grams of Terramycin (brand of oxytetracycline) daily were started. There was a complete absence of neutrophils for three days although the peripheral smear did contain some eosinophils and basophils. On 11 March there were a few juvenile neutrophils (metamyelocytes). By 15 March the white blood cell count and differential had returned to 5 800 per  $\mu$ l with 50 per cent neutrophils, 44 per cent lymphocytes and 6 per cent monocytes.

During the period of granulocytopenia the patient was relatively asymptomatic. By 15 March symptoms of thyrotoxicosis began to reappear: the pulse rate had increased from 90 to 110 and tremor was present again. On 18 March the patient was transferred to the U S Naval Hospital, San Diego, Calif., where she was treated with iodine 131. She has been followed periodically in this clinic and as of 26 October 1957 is euthyroid, clinically well and without evidence of cardiovascular disease.

### DISCUSSION

This patient had had thyrotoxicosis for several months. She was admitted to this hospital without previous treatment and although she had typical signs and symptoms of thyrotoxicosis her major complaints and physical findings were related to the cardiorespiratory systems. At that time it was indeterminate as to whether she had coexisting thyrotoxicosis and cardiac disease, or primary thyrotoxicosis with secondary cardiac signs and symptoms.

Therapy initially was directed toward the thyrotoxicosis and consisted of bed rest, high caloric diet, sedation and antithyroid drugs. Although the patient was bordering on congestive heart failure it appeared that treatment of her thyroid disease would correct her cardiac difficulty. Twenty-four hours following admission she became restless and anxious. The examiner interpreted this as being caused by increased thyroid toxicity, and the patient was heavily sedated but without any particular benefit. It is well documented that a patient with thyrotoxicosis has an increased oxygen demand. In this case the anxiety, apprehensiveness and restlessness were due primarily to congestive heart failure and cerebral anoxia secondary to thyrotoxicosis. This condition has been frequently termed thyroid storm. If immediate steps are not taken to correct the heart failure and oxygen lack the results will be disastrous.

The therapy in this case at the time of the critical period was directed primarily toward cardiac failure and anoxic anoxia. The response was dramatic and the patient required no further sedation for a period of 12 hours and then only small doses of barbiturates. While it is understood that there are many facets to the treatment of a patient with thyrotoxicosis in a critical

state steroids and intravenous dextrose did not seem to be indicated following the patient's response to the above therapy

Propylthiouracil was increased to 1 200 mg per day in order to bring the patient to an euthyroid state as soon as possible Large doses of propylthiouracil have been used by Bartels and Kohn in patients such as ours with good results and no particular increase in side reactions While the improvement in our patient was rapid with the large dose of propylthiouracil the patient did develop granulocytopenia McGavack and Chevalley<sup>4</sup> reported that there is an increased incidence of granulocytopenia (from 0 1 to 0 3 per cent) with doses larger than 150 mg daily The iodine was discontinued because the definitive treatment decided upon in this case was iodine 131

### SUMMARY

A patient with thyrotoxicosis developed signs and symptoms that would be interpreted as thyroid storm The primary cause of the anxiety apprehensiveness and restlessness were cardiac failure and cerebral anoxic anoxia as demonstrated by the fact that she responded to specific therapy directed toward the heart failure and anoxia She approached the euthyroid state very rapidly on large doses of propylthiouracil but developed granulocytopenia which subsided on discontinuance of the drug She subsequently was treated with iodine 131 At the present time she is euthyroid clinically well and without evidence of heart disease Such cases of thyrotoxicosis and impending cardiac failure should be treated as any other case of congestive failure while the primary thyroid disease is being brought under control

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# Mycetoma Pedis

## A Case Report Emphasizing Radiographic Changes

GEORGE F LULL Jr Lt Colonel MC USA

**M**YCETOMA, or maduromycosis, is a chronic granulomatous disease which usually affects the foot but that also has been reported in other parts of the lower extremity, scrotum, trunk, and upper extremity. The disease, though not common, should be of interest to the military services because of its chronicity and because the only hope for cure and rehabilitation lies in its early diagnosis.

While mycetoma is usually thought of as a disease associated with the tropics, it also is found in temperate zones and is world wide in distribution. The first case in the United States was reported by Hyde, Senn, and Bishop<sup>1</sup> in 1896. The incidence in North America is relatively low, but it probably is higher than indicated in the medical literature or in public health reports. According to Quinland and Chenault,<sup>2</sup> a total of 57 cases had been reported to 1950, 19 of these being in the decade 1941-1950. Burns, Moss, and Brueck<sup>3</sup> noted that the number of reported cases seemed to follow the curve of investigation of the subject, and suggested that during periods of low incidence many cases were unrecognized, being classified as chronic osteomyelitis of the foot. This is not unusual, and patients certainly have been separated from the military service with unrecognized mycetomas.<sup>2</sup>

Mycetoma is caused by a large variety of fungi belonging to many species and genera, and by many actinomycetaceae. The greatest number of documented cases in North America were caused by actinomyces or nocardia. The pathologic changes and the clinical course, however, are the same regardless of the etiologic agent, and laboratory studies are necessary to differentiate one infection from another. It was thought originally that specific organisms produced specific colored granules, but it has been shown that a single organism in the same patient can produce granules of different colors.<sup>4</sup> The granules, which may be white to yellow, red or black, are conglomerations of the organisms.

F m Gog H p l A C l Zo Col Lull n w s ign d to Fitz mons  
Army H p l D n er Colo

In the maduromycoses, granules of true fungi are found which contain large segmented mycelium with well defined walls and often chlamydospores. The granules in actinomycoses contain fine nonsegmented filaments with poorly defined walls and no chlamydospores. Even when this distinction has been made further classification may assume some importance, for good results have been reported with sulfanilamide in cases in which the causative organism was nocardia. The difficulty lies in growing the organism on culture media. Green Bolton and Woolsey have pointed out that growing the organism really requires special effort.

The incubation period in this disease is unknown but it may be weeks or months. The inoculation is believed to be a product of trauma although it is not always possible to elicit this history. There are cases reported which were associated with trauma that did not result in a visible break in the skin surface and it is likely that a similar situation prevails in those cases in which no trauma is reported.<sup>3</sup>

The greatest number of cases of mycetoma involve the foot and this is particularly true in areas where shoes are not worn. There are cases with foot involvement in persons who normally are shod however so that the wearing of shoes by military personnel does not preclude their becoming infected if they come in contact with the pathologic organism.

The clinical course is slowly progressive over a period of years. There may be periods of remission but spontaneous cure is rare if it occurs at all. The organisms are aerobic but seem capable of extracting sufficient oxygen from the tissues in which they are located and the initial symptoms may not appear for a considerable period after healing of the original injury.

The early symptoms are pain and tenderness followed by the development of a hard deep seated, nodular lesion accompanied by swelling. The swelling extends peripherally and additional nodules develop. The nodules soften and rupture, with discharge of pus containing the characteristic granules. Drainage may continue for a few days and be followed by healing over of the sinus but the healing is generally superficial overlying superficial or deep seated abscess cavities. Various phases of the process are present at the same time and there is marked fibrosis as the disease progresses over the years. No tissue is spared. Fascial planes offer no barrier and bone is involved as well. The end result is a swollen distorted, globose appendage. The toes are separated and misdirected. This is the result of an increase in the soft parts due to fibrous proliferation with resultant lymphatic obstruction and of fibrous contractures. Pain is present but not excruciating and the major difficulty is one of impairment of locomotion.

There is a paucity of information in the literature with respect to the radiographic changes in mycetoma pedis. Many of the standard texts contain no mention of the disease. Brailsford<sup>6</sup> wrote "Radiographs show marked osteoporosis associated with multiple rounded areas of cancellous destruction which represent foci of infection. The lesions, which may be found in any bones of the foot, may become confluent; they are perhaps most prominent when they involve the metatarsals." Shanks and Kerley<sup>7</sup> were even more brief, and stated that there are no characteristic features. They quoted Benassi and Fiaschi<sup>8</sup> as finding the radiographic changes to be those of osteoperiostitis, with predominating new bone formation. These are the only authors to report this finding. Carroll<sup>9</sup> summarized the changes by stating that the principal findings are cystic destruction of bone, with little surrounding bone reaction, and irregular thinning of the shafts of the metatarsals and phalanges. Carter<sup>10</sup> reported that the bones are diffusely destroyed and barely visible on the film. He further pointed out that when single lesions are presented, there may be little or nothing to suggest mycosis, but that where foci are multiple and varied, a tentative diagnosis may be profitable. Another point mentioned is a striking absence of surrounding bone reaction and sclerosis.

Thirteen case reports in the literature<sup>2, 3, 5, 9, 11-16</sup> were reviewed in an attempt to determine if the mycotic bone lesions were purely destructive or if any cases showed the osteoperiostitis and predominant new bone formation of Benassi and Fiaschi. Of the 13 cases, the bone changes are not mentioned in 1; in 1, no bone changes were present; in 1, the changes described were entirely sclerotic; in 2, there was mixed destruction and proliferation, and in 8 the only changes were those of destruction. In all cases there appears to have been demineralization, which apparently was secondary to disuse and to associated overlying soft tissue inflammatory reaction. Those cases with destructive changes include both simple loss of bone substance, particularly in cancellous bone, and an apparently classical punched out appearance to the bone, particularly in the shafts of the metatarsals and phalanges. This is illustrated in figure 1. The multiple, round areas of bone destruction represent the sinus tracts, and in the smaller bones may show some expansion. If these sinus tracts involve just the bone margin, a half moon effect is produced. The radiographs reproduce the clinically apparent spreading of the phalanges and metatarsals by increased volume of soft tissue. The normal margination and planes of cleavage in the soft tissues are lost. The surface nodularity also is evident on films. In a far advanced case the destruction may result in a lacelike pattern of the remaining bone.





Fig 1. Clinical and roentgenographic application of the general and special at the point of the distal tibia. The punctate area of the tibia is the site of the fracture.

### CASE REPORT

A 26-year-old Panamanian woman sustained an injury to the right ankle in 1942. The initial injury was slow to heal. About one year following the injury she was given surgical treatment elsewhere. The exact nature of this treatment to the right ankle is not known. During the next seven years she had intermittent pain in the leg and toes were present about the ankle. The symptoms had been worse during the six months preceding her initial admission to this hospital in April 1950.

The records indicate that she had received some form of dispensary care during the period 1948-1950 but the physical findings at that time are not known. She was referred to the radiology department of this hospital in July 1948 with a clinical diagnosis of chronic leg ulcer. At that time the roentgenograms showed a marked periosteal proliferation of the distal right fibula (fig 2). The tibia appeared normal and the ankle joint was intact. The changes were interpreted as compatible with chronic stasis and chronic leg ulcer. A second roentgenographic examination 13 months later showed in addition to the periostitis an area of increased density and of rarefaction in the medullary portion of

the fibula (fig 3) The changes were interpreted as a chronic osteomyelitis

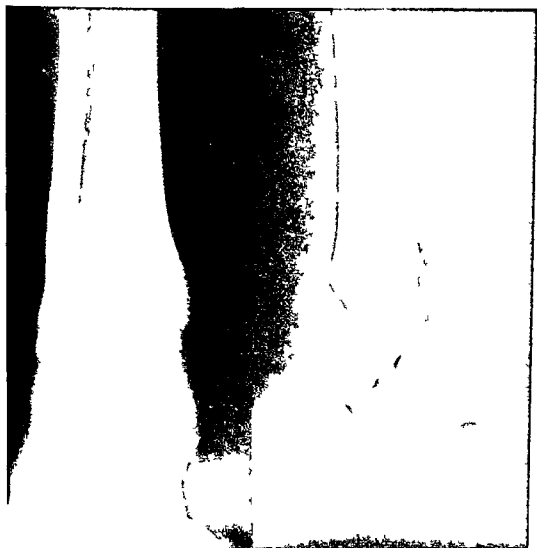


Figure 2 (July 1948) First radiographic changes reported in present case. Note the periosteal proliferation along distal fibula shaft

On admission to this hospital in April 1950 the complaints were pain and deformity in the right leg and foot. On physical examination the right ankle was fixed in equinus and there was resistance to flexion and extension. There were skin changes over both malleoli consisting of depigmentation, scar formation, thinning, and loss of hair. There was a tender, fluctuant area over the lateral malleolus. Draining sinuses developed over the ankle. *Micrococcus pyogenes* var. *aureus* sensitive to streptomycin sulfate was cultured from the discharge. The sinuses became quiescent on antibiotic therapy. Roentgenograms at this time showed considerable change over the outpatient examination in August 1949. An irregular radio-density was reported in the os calcis and it was stated that the changes indicated a chronic osteomyelitis of the os



Fig 1 Clinical photograph of patient with general edema at ankle and foot. The patient has a large ulcer on the medial aspect of the ankle.

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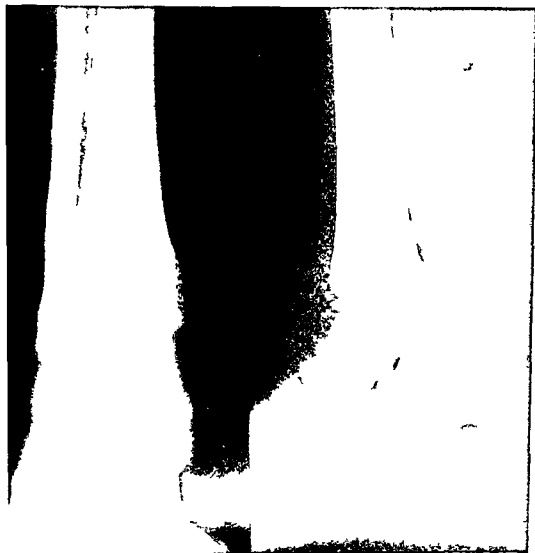


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calcis and distal fibula. After six weeks the patient was returned to dispensary care.



Fig. 3 (Aug. 1949) Progressive changes in 13 months consisting of areas of increased density and architectural modification of fibula. Findings interpreted as chronic osteomyelitis.

The second hospitalization covered the period 27 June 1951 to 16 July 1951 and the clinical picture was a duplication of that seen on the first admission except for evidence of progression. Progressive roentgenographic changes are shown in figure 4. These were described at some length with the conclusion that they represented far-advanced osteomyelitis of undetermined cause with an associated aseptic necrosis of the os calcis.

The final hospitalization was from November 1953 to January 1954. The chief complaint was pain and drainage in the right foot which had greatly increased in size. The skin was reddened, considerable tenderness was present and there were about two dozen draining sinuses over the dorsum of the foot. No motion was present in the ankle. There was an enlarged tender femoral node. The patient had been treated with both antibiotics and sulfonilamide with no improvement.



*Figure 4 (July 1951) Progression of lesion in approximately three years to involve os calcis. Note that process is predominantly proliferative but evidence of sinus tracts is present*

The first films seen by me were dated 13 November 1953. They showed the old periosteal reaction along the right distal fibular shaft. There was marked irregular demineralization of the distal ends of both bones of the leg and all bones of the foot. A fairly large area of bone and joint destruction was present in the mid tarsal area and scattered smaller defects were noted within the several bones of the foot. There was also some irregular condensation of bone most marked in the os calcis. Swelling of the soft tissues was noted. A diagnosis of Madura foot was made (figs 5 and 6).

Biopsy for culture resulted in identification of nocardia as the offending organism. Amputation of the right leg in the proximal third was

The radiographic changes in this case do not fit the classical pattern as shown in figure 1. However in the advanced stages they permitted an accurate diagnosis and there were changes in the os calcis in 1951 which might have suggested mycetoma. It would appear from many of the cases reported in the literature that mycotic infections are purely destructive in their reaction on bone and that the productive bone reaction occasionally seen is due to the stimulation of secondary invaders. In this case *Micrococcus pyogenes* var *aureus* was cultured from the pus on several attempts. Thus the radiologist must be aware of the possibility of obscuration of the true nature of the disease by complicating factors.

## SUMMARY

A discussion of the clinical and radiographic features of mycetoma pedis has been presented with a case report that illustrates the problems and difficulty of diagnosis. While no pathognomonic radiographic changes have been definitely established certain features when present, should suggest the diagnosis. The disease though rare is of world wide distribution and of importance to the military services. It probably is more prevalent than recorded cases would indicate. Because of its low incidence it is not considered in the differential diagnosis of bone lesions as often as it should be and it is believed that inclusion of this condition by the radiologist among the differentials offered may alert the clinician early enough in the course of the disease to permit earlier and more successful therapeutic measures.

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### THE FATHER OF MODERN CHEMISTRY

The year is 1790 the scene is Paris The thunder of the Revolution shakes the earth Yet in the quiet and calm of his laboratory Antoine Laurent Lavoisier is putting a great question to nature He has been told that when substances burn they lose a mysterious material called phlogiston Lavoisier did not believe it He asked How do you know that? If phlogiston exists said Lavoisier I shall get it and weigh it on the balance and compute it by mathematics If I cannot weigh it or compute it by mathematics it does not exist And thus with this spirit of wholesome inquiry he showed that burning was not the dephlogistination of matter but a combining with oxygen And then what about breathing? inquired Lavoisier He described the oxygenation of blood in the lungs and developed the biological chemistry of the pulmonary circulation described by Servetus

But Lavoisier was an aristocrat and the Revolution rabble was in the saddle He was snatched abruptly from his experiments and tried before the revolutionary tribunal Robespierre drew his finger around his neck and declared The republic hath no need of savants On May 2 1794 third in a line of 28 Lavoisier rode in the tumbril over the cobbled streets of Paris to the Place de la Concorde The guillotine fell Lagrange very trenchantly commented It took but a minute to sever that head France will be a century in producing another like it This statement was prophetic because France did not produce another citizen like Lavoisier until the advent of Louis Pasteur With the simplicity to wonder he has been fittingly called the father of modern chemistry "

—JOHN C KRANTZ Jr  
in *Connecticut State Medical Journal*  
p 828 Sept 1957



## Departments

### PRESIDENT EISENHOWER IS MADE HONORARY FELLOW OF AMERICAN COLLEGE OF SURGEONS



In a White House ceremony on 6 February President Eisenhower was made an honorary fellow of the American College of Surgeons. He is shown above wearing the hood of the College. Left to right are Major General Howard McC. Snyder, USA (Ret.), White House physician Dr. Brian Blades, Professor of Surgery, George Washington University School of Medicine; Major General Leonard D. Heaton, MC USA, Commanding General, Walter Reed Army Medical Center; Dr. John H. Lyons, Washington, D. C., the President; Dr. I. S. Ravdin, Professor of Surgery, University of Pennsylvania School of Medicine and Chairman of the Board of Regents of the College, who read the citation on the President; Dr. Frank B. Berry, Assistant Secretary of Defense (Health and Medical); and Robert Cutler, special assistant to the President for National Security Affairs, and president of the board of trustees of Peter Bent Brigham Hospital, Boston.

## ADM KENNEY NAMED ASSISTANT BUMED CHIEF, SUCCEEDED AT BETHESDA BY CAPTAIN KREUZ

Rear Admiral Edward C Kenney, MC USN, recently promoted to flag rank has reported for duty as Assistant Chief for Personnel and Professional Operations, Bureau of Medicine and Surgery Department of the Navy. A combat veteran of World War II, Admiral Kenney was awarded the Navy Cross for extraordinary heroism while serving as senior medical officer of the U S S *Boise* and the Bronze Star Medal with combat "V" for meritorious service while participating in landings on Guam, Leyte and Lingayan Gulf.



*Rear Admiral Thomas F. Cooper, MC USN, right, Commanding Officer of the National Naval Medical Center, congratulates Rear Admiral Kenney on his promotion.*



*Captain Kreuz.*

Captain Frank P. Kreuz, MC USN, has succeeded Admiral Kenney as Commanding Officer of the U S Naval Hospital Bethesda, Md. A diplomate of the American Board of Orthopedics since 1948, he has served as chief of the orthopedics services at the U S Naval Hospitals in Philadelphia and Bethesda. During World War II, he was senior medical officer on the staff of the commander, Battle Force Pacific, aboard the U S S *Washington* and was awarded the Bronze Star. His most recent assignment was Commanding Officer of the U S Naval Hospital Guam.

## BRIG GEN M S WHITE INSTALLED AS PRESIDENT OF AERO MEDICAL ASSOCIATION

Brigadier General M S White USAF (MC) was installed as president of the Aero Medical Association at the conclusion of the Society's 29th annual meeting in Washington D C 1st month

Captain Ashton Graybiel MC USN Director of Research with U S Naval School of Aviation Medicine Pensacola Fla outgoing president of the Association directed the activities of the three-day meeting on March 24 25 and 26 which attracted nearly 1500 aeromedical scientists from thirty countries More than 100 speakers in the extensive scientific program presented research advances directly related to the biologic aspects of flight and particularly the conquest of outer space



General White

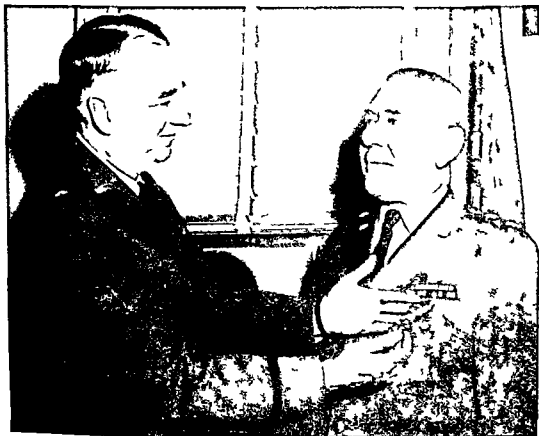
The Association's Theodore C Lyster Award for outstanding achievement in the field of aviation space medicine was won by Dr Hubertus Strughold Medical Research Advisor to the Commandant of the Air Force School of Aviation Medicine Dr Siegfried J Geathewohl was the recipient of the Arnold D Tuttle Award Brigadier General Victor A Byrnes and Colonel Harry G Mosely USAF (MC) received the Eric Liljencrantz and Raymond F Longacre Awards respectively

Captain Oran W Chenault MC USN and Colonel Benjamin A Strickland Jr USAF (MC) were elected members of the Executive Council for a three-year term Military physicians advanced to the grade of fellow include Rear Admiral Winfred P Dana MC USN (Ret) Captain Norman L Barr William M Snowden and Carl F Wilbur MC USN Colonel Charles H Roadman USAF (MC) Major David G Simons USAF (MC) and Dr Hubertus Strughold Dr Howard T Karsner Research Advisor to the Surgeon General of the Navy was elected an honorary fellow

A flight surgeon for more than 20 years General White is Director of Medical Staffing and Education for the Air Force Surgeon General In 1940 he made the first electrocardiograph recordings and the complete scientific study of heart action of pilots during high altitude flight This study led to the development of technique for the recording of biological functions which are now widely used in the investigation of human factors in flight In 1945 he was a member of the Air Force group which pioneered the first scheduled round-the-world military air transport flights in six days

## GEN KENNEBECK, AIR FORCE DENTAL CHIEF, RECEIVES LEGION OF MERIT ON RETIREMENT

Major General Marvin E. Kennebeck, Assistant for Dental Services, Office of the Air Force Surgeon General, was awarded the Legion of Merit in retirement ceremonies on 31 January 1958. Brigadier General James S. Cathroe is the new Assistant for Dental Services.



*Major General Dan C. Ogle, Air Force Surgeon General, presents Legion of Merit to Major General Kennebeck.*

General Kennebeck, an early advocate of the fluoridation of water supplies at Air Force bases, was appointed Assistant for Dental Services in June 1952. He initiated the Air Force Preventive Dentistry Program which has contributed immeasurably to the high health standards of the Air Force and introduced the panoramic dental x-ray machine and the use of chrome cobalt alloy to replace gold in dental work. During General Kennebeck's Washington assignment, dental-officer and post-graduate training was more than doubled to afford the highest type of professional training to Air Force dental officers. General Kennebeck was born in Carroll, Iowa, and received the degree of doctor of dental surgery from the University of Iowa in June 1924. He entered on active duty on 9 September 1924 as assistant dental surgeon at Walter Reed Army Hospital. He is former president of the Armed Forces Commission of the *Federation Dentaire Internationale* and past vice-president of the American Dental Association.

## WHO CELEBRATES TENTH ANNIVERSARY

On April 7 the traditional date of World Health Day the World Health Organization observed its tenth anniversary



Dr. A. G. Candau

This day provides an excellent opportunity to review the strides made towards our goal of the highest possible level of health during the past decade of national and international effort said Doctor M. G. Candau, Rio de Janeiro, Brazil, director-general of WHO. There have been great scientific advances during this period and this new knowledge is being rapidly applied where it is needed. In the last 10 years the flow and exchange of scientific information and practical experience have perhaps been greater than ever before. More scientists and health workers than ever before have gone from country to country to learn to teach and to demonstrate.

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### Russian Medical Translations Available

The Pergamon Institute, a nonprofit foundation, was recently formed in Washington, D. C. and London for the purpose of making available to English speaking scientists, doctors and engineers from United Nations countries the results of scientific, technological and medical research and development in the Soviet Union and other countries in the Russian orbit. More than 100 scientists of international standing have given their support to this project and will supervise the affairs of the Institute. Dr. Detlev W. Bronk and Sir Robert Robinson, O. M., F. R. S., are joint presidents of the Institute's board of governors.

The Institute publishes in English the following Russian medical journals: *Biophysics*, *Sechenov Physiological Journal*, *Problems of Virology*, *Problems of Hematology and Blood Transfusion*, *Journal of Microbiology*, *Epidemiology and Immunobiology*, and *Problems of Oncology*. These periodicals and other selected translations including microcards and microfilms are available to individual physicians and scientific societies.

The Institute plans to hold a symposium during the summer of 1958 either in Washington or London. Additional information can be obtained from the Pergamon Institute, 122 East 55th Street, New York 22, N. Y.

## Medical Writing Award Announced

The editors of *Modern Medical Monographs* a quarterly publication, announce an award for the best unpublished manuscript for a short book on a clinical subject in the field of internal medicine. The purpose of this award which will be known as the Modern Medical Monograph Award is to stimulate young physicians to communicate their work in the classical form of the monograph and to achieve high standards of medical writing. The winner of this competition will receive \$500. In addition the winning monograph if found suitable will be published as a book in the series *Modern Medical Monographs*.

The entries will be judged for style and clarity of expression by a committee of the American Medical Writers Association and for clinical interest and scientific value by the editors and advisory board of *Modern Medical Monographs*. The award will be governed by the following rules:

- 1 The author or authors must be a graduate physician less than 40 years of age. Single authorship is preferred but two coauthors will be acceptable. The name of the medical school from which the author graduated and his date of graduation should be stated.
- 2 Manuscripts should be submitted in duplicate (original and one copy) by registered mail postmarked no later than October 1, 1958 to Richard H. Orr, M.D., 37 East 67th St., New York 21, New York.
- 3 The manuscript including the bibliography must consist of between 115 and 200 double spaced typewritten pages with ample margins and not more than 40 illustrations (figures or photographs). For each illustration used the allowable upper limit of typewritten manuscript pages should be reduced by one.
- 4 Fishbein's book *Medical Writing* (third edition) should be followed in preparation of the manuscript use of abbreviations and bibliographic form.

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## ARMY ENDS SHIPMENT OF BOOKS TO KOREA

The American Korean Foundation and the United States Army Medical Service have announced the discontinuance of their joint project of shipping medical books contributed by individual physicians, medical schools, hospitals, and state and local medical societies to Korea. Books should not be sent to the Sharpe General Depot in California as in the past because facilities no longer exist for packing and transshipping to Korea.

In making this announcement Howard A. Rusk, M.D., Chairman of the American Korean Foundation, said: "The response of physicians and medical groups throughout the country to our appeal for books for Korean medical schools has been so generous that such further contributions are no longer needed."

# OFFICERS CERTIFIED BY SPECIALTY BOARDS

## Supplementary Listing

The following regular Medical and Dental Corps officers have been certified by the boards indicated since the listings published in previous issues of this *Journal* according to information from the Offices of the Surgeons General of the military medical services

### American Board of Pediatrics

Edwin A. Mink M J USA

### American Board of Psychiatry and Neurology Psychiatry

Merritt B. Gifford Lt. Col USAF  
B. Harrington M J USA

### American Board of Orthopaedic Surgery

Fredrick R. Hick M J USAF

### American Board of Dermatology and Syphilology

Charles H. Williams M J USA

### American Board of Radiology

William W. B. D. rz Cap USAF

### American Board of Pathology

John G. Webb Cpt. USAF

### American Board of Surgery

B. J. Minner R. B. k M J USAF  
John A. B. l M J USAF  
De M. R. g M J USAF  
E. an W. S. h L. C. l USAF  
J. b F. S. hirm L. C. l USA  
J. h. H. Sh. p Lt. Col USA

### American Board of Anesthesiology

H. man R. Ha M J USA

### American Board of Prosthodontics

Clifford W. S. Lt. Col USA

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## DEATH

NOVAK, L. u. ( ) Chief Medical Serv. W. Off. USN. f. Ph. l.  
d. lph. P. stat. d. t. th. U. S. Mar. C. rp. R. rust. D. p. t. P.  
I. l. d. S. C. d. a. th. U. d. S. t. N. vy. i. an. l. t. d. t. t. f. m.  
9 April 1931. t. l. 15 J. ary 1944. pp. t. d. Pharm. th. U. t. d.  
St. t. N. vy. 16 J. ary 1944. d. d. 17 February 1958. g. 44. t. th. U. S.  
N. l. H. p. tal. B. f. r. t. S. C. f. ca. m. f. th. lung.

## WHITE HOUSE DOCTORS

One of the feature articles in *MD Medical Newsmagazine* which made its debut a year ago is entitled *White House Worriers*.<sup>1</sup> It struck your Observer as a rather apt title for a dissertation on Presidential physicians.

Any physician responsible for the health of a prominent individual is constantly aware that his ministrations are under close scrutiny. This is especially true when the patient happens to be the President of the United States.

The century and a half during which physicians have served Presidents covers nearly the whole medical history of the United States "from the blood letting of Washington to the electrocardiography of Eisenhower." Illustrative of the professional relationships and medical progress are sketches of selected Presidential physicians who have watched over a President's health in war and peace. These are James Craik (1730-1814), Philip Syng Physick (1768-1837), Robert King Stone (1822-1872), Benjamin Fordyce Barker (1818-1891), Ross T. McIntire (1889—) and Howard McCrum Snyder (1881—). Drs. Physick, Stone, Barker, McIntire and Snyder were or are members of the Medical Society of the District of Columbia.

Like Dr. Snyder, the present White House Physician, Dr. Craik had been closely associated with the President he served before he took office. He was with General Washington in the war against the French and later the British.

By modern standards, Dr. Craik's methods were crude. MD states he knew no other remedy than blood letting, gargling with vinegar and sage tea, and the application of Spanish Fly (*Cantharis*, the blister bug) to the throat. He treated the President for a variety of respiratory conditions, carbuncles, inflammation of the eyes, and recurrent malaria. His consultants were Drs. Flisha Dick and Gustave Brown. They knew little more than he did.

Dr. Physick practiced during the same period. It appears that he had a recalcitrant patient in President Andrew Jackson. Wild and hot tempered, the soldier-lawyer rode roughshod over medical advice, placed his faith in lead acetate for practically any ailment. He was one of a legion of patients before and since who knew better than his physician what was wrong with him. However, he had a wholesome respect for Dr. Physick because of the high regard in which he was held professionally. Nevertheless, he protested: "I can do anything you think proper except give up coffee and tobacco."

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<sup>1</sup> Reprinted with permission from *Medical Annals of the District of Columbia* 27: 85-86 Feb. 1958.



President Jackson suffered from chronic pleurisy due to a bullet lodged in or around the pericardium received in a duel in 1806. Dr. Physick's chief remedy for pleurisy was cupping. He also prescribed freely heroic doses of lead acetate and calomel to prevent the President's self-treatment.

Dr. Stone was President Abraham Lincoln's personal physician. Lincoln usually ignored his doctor's prescription of shorter work hours and longer bed rest. He suffered from hypochondria then attributed to defective digestive functions. This contributed to melancholy which dripped from the tall gaunt man.

Chronic constipation, a sluggish circulation, a poorly functioning liver, an apparent deviation of the left eye, and a suspected tendency to tuberculosis were conditions for which President Lincoln was treated. A remedy prescribed by one of Dr. Stone's predecessors for the President's general condition was blue pills (mercury mass).

President Ulysses S. Grant sought out Dr. Barker as his physician. There was a satisfying personal relationship. He treated the President for malignancy of the throat. The treatment consisted of the application of a solution of muriate of cocaine (4 to 12 per cent) two or three times a day. Potassium permanganate and brewer's yeast were used in gargles. Iodoform was applied to the diseased tissue by insufflation.

The diagnostic procedures followed and therapy prescribed by Dr. Snyder address as catalysts in the treatment of President Dwight D. Eisenhower as compared with those of his predecessors. Illustrate the phenomenal progress of medical science. Time too has wrought great changes with respect to the secrecy which in the past surrounded the affliction of Chief Magistrates. No longer is there any attempt to conceal even the elemental physiologic processes which relate to the President's health.

One may question the good taste or even the necessity for these revelations, but where the President's physician is concerned, frankness relieves him of the burden imposed by secrecy. It offers him an opportunity to disclose who the consultants are, their professional standing, and their views with respect to the state of the President's health. In his position, he cannot afford mistake, for they will not be overlooked nor excused. So he surrounds himself with the ablest consultants to confirm, modify, or reject his findings.

All in all, for the White House doctor, this is a far better day. He has at his command diagnostic aids and therapy undreamed of by his predecessor. As a result, he should worry less and sleep better nights.

#### REFERENCE

1. White House. *MD M d News* 1: 20-26 Feb 1957.

## A MESSAGE FROM THE A M A

Since 1952, the Council on National Defense of the American Medical Association has conducted an opinion survey among physicians being released from active military service. The questionnaire used in the survey is primarily designed to obtain pertinent data based on the physician's observations and opinions while in the Armed Forces concerning the utilization of physicians and the medical staffing conditions in the uniformed services. The questionnaire also is designed to elicit comments and suggestions as to further improvement of military medical services as well as ways and means whereby organized medicine can be of greater assistance to military physicians.

This report covers the period 1 January 1956 to 31 December 1956. During that period the Council sent out 2,519 questionnaire forms. Of these, 1,600 were completed and returned, representing a 64 per cent response.

**Age Distribution of Responding Physicians.** About 40 per cent (644) of the physicians replying were in the 30-34 year age group. In the 25-29 year age group there were 584 (about 37 per cent) while in the 35-39 year age group there were 284 (11 per cent) of those responding.

**Date of Graduation From Medical School.** More than half of the responding physicians were graduated from medical school subsequent to 1949, the second largest group, about 36 per cent, graduated during the period 1945-1949. None failed to indicate the year of graduation from medical school.

**Years of Residency Training.** The largest group (410 physicians or about 26 per cent of those replying to this question) had no residency training while the second largest group (308 physicians or 19 per cent) had but one year of residency training at the time of entrance on active duty. There were 223 (14 per cent) who had two years, 277 (17 per cent) who had three years and 159 (10 per cent) who had four years of residency training.

**Occupation at Time of Entering Service.** The largest groups of physicians who served in the Army and Navy (24 and 27 per cent respectively) were engaged in general practice at time of entrance on active military duty while the largest group in the Air Force (36 per cent) was in internship. The summary report for the year 1955<sup>1</sup> showed that the largest groups in the Army and Air Force were engaged in general practice while the largest group in the Navy was in residency training prior to active military service.

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<sup>1</sup> From the Council on National Defense of the American Medical Association. The  
work of physicians prior to entry into the Department of Defense  
—Ed to

**Number of Physicians Holding Board Certificates** Of the 993 persons responding to the question 131 holding specialty board certificates were in the Army 125 were in the Navy and 37 were in the Air Force The specialties covered over 19 different fields of which the largest was internal medicine the second largest was surgery and the third largest was pediatrics In the previous report for the year 1955 internal medicine was first followed by pediatrics and surgery By branch of service a total of 22 per cent of those responding in the Army 20 per cent of those in the Navy and 10 per cent of those in the Air Force had specialty board certificates

**Government Medical Education Received** A total of 533 of the 1 600 physicians responding stated that they had received assistance in their medical education from the Federal Government while 1 067 indicated they had received no Government assistance The largest single group receiving Government assistance was under the Army Specialized Training Program The next two largest groups were under the Navy V 12 Program and the GI Program Of the responding physicians 64 per cent of those who served in the Army 67.3 per cent of those in the Navy and 70 per cent of those in the Air Force received no Government assistance

**Training Received While in Service** There were 895 of the physicians responding who received military medical training while on active duty in the Army Navy or Air Force The Medical Field Service School accounted for 602 the largest number while 156 the second largest group received training at the School of Aviation Medicine In the Army group about 82 per cent received the Basic Course training of the Medical Field Service School as did nearly 8 per cent of those in the Navy and 24 per cent of those in the Air Force

**Physicians Evaluation of Military Medical Training** The great majority of physicians filling out the questionnaire thought that all important features of military medical training had been satisfactorily covered For the Army 82 per cent were satisfied with the training while 67 per cent of those in the Navy and 85 per cent of those in the Air Force were satisfied A small percentage indicated that the training was unsatisfactory but gave no specific reasons Others stated reasons why they considered their tour of service unsatisfactory Most of these physicians in the Army and Air Force reported insufficient training in military customs administration and regulations as an unsatisfactory aspect of military medical training while most Navy physicians reported insufficient basic orientation and indoctrination

**Physicians Evaluation of Assignment** The vast majority of responding physicians stated that their longest and next longest

assignments were almost completely or partially but satisfactorily, in line with their training and experience. With respect to the longest assignment, 80 per cent of the Army physicians, 73 per cent of the Navy, and 87 per cent of the Air Force physicians replying were of the opinion that the assignment was almost completely, or partially but satisfactorily, in line with training and experience. In regard to the next longest assignment the percentages were 72, 75 and 78 per cent respectively, for the favorable opinions of Army, Navy and Air Force physicians. Consistent with this evaluation, the vast majority also expressed satisfaction with the same assignments. In answer to both questions a greater portion of the Air Force physicians responded favorably than did Army or Navy medical officers.

**Types of Patients Treated** One of the questions was designed to determine the percentage of time devoted by physicians to military personnel, dependents of military personnel and administrative duties, both at domestic and overseas stations. On assignments in the United States nearly 47 per cent of the reporting physicians devoted one half or more of their time to the treatment of military personnel, while nearly 39 per cent devoted one half or more of their time to the treatment of dependents of military personnel. At overseas stations nearly 30 per cent of the physicians replying devoted one half or more of their time to military personnel and 12 per cent devoted one half or more of their time to dependents of military personnel.

**Types of Nonmilitary Medical Care Provided** The question that was designed to determine the types of medical duties most frequently performed for nonmilitary persons elicited the information that in all three of the armed services outpatient care ranked first at domestic and overseas stations. In the Army general medical and hospital care was second in the United States, while pediatrics was second at overseas stations. In the Navy pediatrics was second at domestic installations while general medical and hospital care was second overseas. Obstetrics and gynecology was second for Air Force physicians in the United States and pediatrics was second at overseas bases.

**Medical Care of Dependents by Civilian Medical Personnel** With respect to service in the United States, the great majority of responding physicians were of the opinion that all medical care of nonmilitary persons could have been adequately performed by civilian military personnel. In the three military services 816 of 1,316 physicians (62 per cent) so responded. In regard to overseas service, however, only 127 of 495 physicians (26 per cent) were of that opinion.

#### REFERENCE

## CORRESPONDENCE

N G P i i g

*To the Editor* —I have been interested in the paper which appeared on page 1726 of the December 1957 number by Oberst et al. on the use of the Batrow neuromuscular stimulator in GB poisoned animals. I am very puzzled however that nowhere in the article was there any discussion as to why this form of stimulator as well as the Sarnoff stimulator could not possibly work.

In both curare poisoning and poisoning by such cholinesterase depressants as GB nerve gas the pathology is a transmission failure from motor nerve to muscle due to the myoneural junction. If the normal nerve impulse is unable to get across and contact the muscle it is absurd to expect that the nerve impulses produced by an electric current could work. Both of the stimulators mentioned in this article are effective in stimulating the motor nerve through their faradic properties. In the case of a rapid reversal of electric current in the case of the Sarnoff stimulator 60 times a second and in the case of the Batrow stimulator a short pulse of only 7 milliseconds in duration that is produced 60 times a second. Denervated muscle by means of chemical block at the end plate can only respond electrically to a direct current type of stimulator which has so far not been designed for as far as I know. There is ample evidence in the literature and in the experience of clinicians that in polyneuritis curare poisoning myasthenia gravis and in nerve gas poisoning the muscle will not respond to stimulation of the motor nerve. This is not true in drowning poliomyelitis or paralysis of breathing due to increased intracranial pressure or damage to the medulla and spinal cord. Both of these stimulators were designed and recommended for this kind of respiratory difficulty where the peripheral part of the motor nerve is equipped with a normally transmitting motor end plate.

I think it is exceedingly important that readers of the *Journal* understand clearly the reason why electrophonic respiration can never work in motor end plate disturbance or instances where the peripheral part of the motor nerve is not functioning and that they were never expected or intended to be effective here. This paper in no way vitiates the success of these stimulators in the types of respiratory difficulty mentioned above where the motor end plate is intact.

ROBERT S. SCHWAB, Chairman, MC USVR (Rt.)  
 Medical Consultant, General Hospital  
 Bethesda, Md.

*Doctor Schwab's letter was referred to Doctor Oberst who made the following comment after consulting with his co workers*

*To the Editor* —We agree with Dr Schwab that when the neuromuscular junction is degenerated or blocked electro-stimulation of the nerve cannot cause muscular contraction Our experiments described in our article show that under controlled conditions we were unable to induce artificial respiration in GB poisoned dogs and monkeys with the Batrow neuromuscular stimulator The equipment did produce unselected muscular contractions but this did not move sufficient air for survival of the animals Doubtless this type of stimulation cannot set up the reciprocal innervation required for respiration to be effective

FRED W OBERST *Ph D*  
U S Army Chemical Warfare Laboratories  
Army Chemical Center Md

#### Asian influenza

*To the Editor* —We have read with interest the article by L S Greene and T A Hair Jr on "Clinical Experience With 682 Cases of Asian Influenza" which appeared on pages 385 to 390 of the March 1958 issue of the *U S Armed Forces Medical Journal* There now is available certain additional information concerning this outbreak that may be of value to your readers and serve to place the article in true perspective

The final Epidemiological Report submitted to the Bureau of Medicine and Surgery Department of the Navy indicated that a total of 1891 cases occurred at the Naval Air Station Memphis Tenn during the epidemic with an attack rate of 16.7 per cent Those cases having severe prostration or fever of 100° F or over at the time first seen were transferred to the hospital The clinical characteristics discussed in this article therefore represent the findings in approximately 35 per cent of the total cases with the remainder presumably having had a milder disease free of significant complications While not detracting from the value of the article to physicians working in hospitals this points up the quite different impression of a disease to be gained by a physician cognizant of the total series of cases The distribution of fever frequency of complications and other characteristics found in a hospital series of patients thus cannot be considered as characteristic of the disease

The reports further indicated that most immunization was not given until after the beginning of the epidemic Medical Department personnel

who received the intracutaneous immunization in advance of other personnel on the station had a much lower attack rate despite their heavy exposure

In the absence of controls this does not provide unequivocal evidence but is suggestive of the fact that the vaccine may have decreased the frequency of acquiring the disease even if not modifying it once acquired. However the general impression of medical officers in the Dispensary of the Air Station was that the vaccine had little effectiveness despite the above finding in Medical Department personnel

HOWARD K. SESSIONS, Captain, MC USN  
 Director, Preventive Medicine  
 JOHN R. SEAL, Captain, MC USN  
 Head, Communicable Diseases Branch

Branch of Medicine and Surgery  
 Department of Health, Navy, Washington, D C

## Medical Education Week April 20-26

The third annual Medical Education Week will be observed 20-26 April throughout the United States to focus attention on and inform the public of the ever increasing contribution of medicine to American life and of the basic significance of medical education. The general objectives of this observation are to develop public understanding of the progress, aims, and problems of medical education in the hope of stimulating more adequate financial support. The committee of organizations sponsoring Medical Education Week include Lowell T. Coggeshall, M D, president, Association of American Medical Colleges; David B. Allman, M D, president, American Medical Association; Louis H. Bauer, M D, president, American Medical Education Foundation; S. Sloan Colt, president, National Fund for Education; Robert Rakel, president, Student American Medical Association; and Mrs. Paul C. Craig, president, Women's Auxiliary to the American Medical Association.

## Reviews of Recent Books

THE BASES OF TREATMENT by *Newton S Stern A B M D* and *Thomas N Stern M D* 176 pages Charles C Thomas Publisher Springfield Ill 1957 Price \$4.75

This book is the outgrowth of a course in therapeutics given by the authors at the University of Tennessee College of Medicine. The subject is approached from the point of view of presenting the principle upon which all therapy is based rather than outlining in detail specific treatment of various disease states. Thus the book should serve as a useful guide to the medical student and practitioner alike for many years even though specific therapeutic agents may change.

The publication of such a volume at this time appears particularly appropriate because it stresses the general symptomatic care of the patient which is so often overlooked in this era of specific remedial agents. It is one which the physician could well have in his library to pick up and read from time to time with a view to refreshing himself on the general principles which should be kept in mind in administering to the sick. —GEORGE M POWELL, Col MC USA

SURGICAL TECHNIQUE and Principles of Operative Surgery by *A. V Par-tip lo M D F A C S* Foreword by *Alton Oschsner M D F A C S* 6th edition 966 pages 1235 illustrations on 719 figures 4 in color Lea & Febiger Philadelphia Pa 1957 Price \$20

Surgeons acquainted with previous editions of this work will anticipate and discover a still greater contribution to surgical technique in the sixth edition. In 38 completely new chapters and the 43 revised chapters the reader will find detailed technics of every significant surgical procedure he will ever employ.

Pragmatic discussions of fluid therapy, transfusions, anesthesiology, radioisotopes, radiation therapy, and suturing are presented prior to the chapter on operative technics. In discussion of a given procedure ample consideration is accorded the indications for surgery, the risk, and the pre and postoperative management. Of particular merit are the 1235 illustrative line drawings of operative procedures, anatomic principles, and physiologic considerations. Reasons are presented step by step for the operative maneuvers. In a review of basic surgical information and operative principles, students, residents, and practicing surgeons will find valuable questionnaires concluding each chapter invaluable. The objectives of this stimulating book have been commendably achieved by the author, namely, the review of (1) pertinent surgical anatomy, (2) essential physiology, (3) correlated pathology, and (4) fundamental clinical aspects of each subject. There is timely emphasis on the importance of diagnosis and valid indications for a given procedure.

This is truly a functional book covering all important aspects of surgery of the neck, the chest, the heart, and great vessels, the abdomen,



and related specialties its extreme usefulness derives from the point by point description of a sound and tested procedure exactly as it is performed by a great teacher —JAMES B ANDERSON Lt Col USAF (MC)

THE INFANTILE CEREBRAL PALSIES by E C H et al 100 p g  
Charles C Thomas P bl h r Sp g t ld Ill 1957 P c \$3

In exactly 100 pages this book covers an amazingly wide range of topics concerning cerebral palsy ranging from the fascinating story of William Little's classical descriptions of the disease to a detailed plan for the organization of cerebral palsy services

The authors are members of the Little Committee formed 100 years after Little's original description of this entity for the purpose of studying the clinical problems of diagnosis prognosis management and the administrative problems involved in training medical and other personnel for work in the field of cerebral palsy They describe a dynamic educative process in which the day-to-day work is carried out by the combined efforts of the child and his mother the cerebral palsy service giving the required advice and encouragement

Separate chapters are devoted to the different forms of cerebral palsy and each chapter includes a typical case history with the details of management appropriate to it and the manner in which advice is given to the mother The raison d'être of this small well-written book is to offer a practical guide for those concerned with the panoply of problems caused by cerebral palsy —THOMAS E CONE J Capt. MC USN

THE CLINICAL APPLICATION OF ANTIBIOTICS by M E Fl ey M D  
Volume III Chloramphenicol tetracycline 393 p g ill  
L. D. O. F. D. U. ty P N w Y k N Y 1957 P \$19 50

This volume is a continuation of the author's earlier work *Clinical Application of Antibiotics*—Penicillin published in 1952 evaluates critically the data on which the present use of antibiotics was founded Chloramphenicol and the tetracyclines (chlortetracycline or aureomycin oxytetracycline or tetracycline and tetracycline or achromycin) are covered in this volume Each is dealt with separately and evaluated in three different categories with a chapter devoted to each The first chapter includes the general consideration such as origin and properties antibacterial action complications of therapy results of clinical trials and administration The middle chapter deals with the treatment of disease due to a specific organism such as rickettsial diseases viral diseases diseases caused by bacteria venereal diseases and tropical and miscellaneous diseases The last chapter for each drug covers the treatment of diseases considered by system age group or sex This includes diseases of the cardiovascular system lungs and bronchial infections within the abdomen obstetric and gynecologic conditions infections in infancy genitourinary infections otolaryngologic infections infections of the skin infections of the eye and bacteremia

The author has covered in detail each of the drugs under consideration by an extensive review of the literature. The effectiveness and routes of administration and complications are discussed. The results of clinical trials are summarized for each drug, showing the specific infections which are consistently responsive, those which have variable response or no response, and also those conditions in which the substance was ineffective in a trial of treatment. This volume is considered excellent for those interested in a review of the literature for each of these individual drugs and an evaluation of their usefulness and effectiveness in the treatment of patients. For the average physician, however, it is too detailed to be read completely, but would make an excellent source of reference for any individual disease or infection where treatment with one of these antibiotics is being considered. —DOSSO LYNN Col MC USA

CLINICAL ORTHODONTICS. A Guide to the Sectional Method by *Bercu Fische*. D D S 478 pages 1332 illustrations on 354 figures W B Saunders Co Philadelphia Pa 1957 Price \$17

The author tactfully relates his experiences in the practice of orthodontics, adhering to his postgraduate training in the aspects of Angle's teachings, which was basically a classification of diagnosis en masse, tooth movement in treatment, and the sanctity of a full complement of teeth. Dissatisfaction with orthodontic results obtained and individual barriers encountered caused the author to search for the reasons and a solution. This led to personal clinical research and a break from Angle's concepts.

The author clearly describes his reasons for divergence from the impact of Angle's concepts upon clinical practice. He outlines in detail clinical data and conclusions to substantiate a new approach in orthodontic treatment based on the individual. Clinical research dictated that diagnosis be made after complete consideration of the individual. Heredity, asymmetries, dentofacial complex, tissue tolerance, arch approximation, compensatory adjustment, and functional adaptation are factors of human individuality that are specifically its own. Individual variability becomes the basis of diagnosis. A diagnosis based on individual variables is then treated sectionally, with or without tooth extractions, establishing the corrected denture as close as possible to the patient's individual functional pattern, maximum stability, and to dental and facial esthetics.

The author's methods of diagnosis and recording are described with the use of numerous illustrations, drawings, and photographs. A chapter devoted to appliances and techniques also is amply illustrated and diagrammed. Another chapter contains an atlas of case reports which analyze clinical procedures in sectional orthodontic treatment.

Although dealing with a controversial subject, this book is well written and ably presented as a new approach to the basic principles

movable appliances for the correction of malocclusion are presented. The quality of paper, the printing style, and the reproductions are excellent. This book should be invaluable for advanced students and dentists interested in orthodontics. —GEORGE H. PARROT, LL.C., DC, USA.

CORTISONE IN DENTISTRY by Ly P. St. M. S. Ph. D. D. D. S.  
F. A. P. H. A. 178 p. g. 57 il. t. t. D. t. l. l. t. m. f. l. t. t.  
P. b. l. h. g. C. I. B. k. l. y. N. Y. 1957 P. \$5.95

The author of this small volume discusses the physiology of the adrenal cortex and its relationship with the anterior pituitary, including the chemistry and biochemistry of cortisone, hydrocortisone, corticosterone, and ACTH. He emphasizes the antirheumatic and anti-inflammatory properties of these substances and their effects on metabolism. The uses of the adrenal cortical hormones have been well established, and this section of the book enables the dental practitioner and dental student not only to become acquainted with their use in systemic diseases but gives them an excellent background for their application in many oral diseases.

The need for such a book has been evident for many years, and it is a revelation to read of the many applications of these stress hormones in oral diseases. It is well written in a clear, concise, and easily readable style. Illustrations, tables, and graphs are clear and pertinent. An adequate bibliography for further reference is contained at the end of each chapter, and a selected list of dental references on cortisone is included. This book should be in all dental libraries and is a necessity for the practitioner of dentistry.

—THEODORE E. FISCHER, C.I., USAF (DC)

INTEGRATING THE APPROACHES TO MENTAL DISEASE Tw. C. f. r.  
H. l. d. d. h. A. p. f. t. h. C. m. m. o. P. b. l. H. l. t. h. f. Th.  
N. w. Y. k. A. a. d. m. y. f. Med. d. t. d. by H. D. Krus. M. D. 393  
p. g. P. l. B. H. b. I. M. d. l. B. k. Dep. f. H. p. & B. o. t. h.  
N. w. Y. k. N. Y. 1957 P. c. \$10

This is the well-edited report of two conferences in which leading exponents of the organic, experimental, psychological, psychodynamic, and psychosocial approaches to understanding mental illness exchanged views in an effort to more clearly define areas of agreement and areas of disagreement, and to encourage research with broad objectives of integration of the various approaches. These worthy objectives and the list of participants doubtless led to unrealistic expectations on the part of this reviewer, because the real value of such conferences can probably never be captured in print. The book contains brief expositions of the positions on etiology of mental disease of each of the four disciplines represented, and a well-documented example of some of the difficulties to be overcome in the multidisciplinary approach to understanding this complex problem of human behavior. It will be of interest to anyone doing research in this field and worthy of careful study by those undertaking multidisciplinary evaluation of any aspect of the problem. —MARION E. ROUDEBUSH, Capt. MC, USN.

**TUMOR SURGERY OF THE HEAD AND NECK** by *Robert S Pollack* M D  
F A C S 101 pages 112 illustrations on 49 figures Lea & Febiger  
Philadelphia Pa 1957 Price \$5

This book contains an interesting and practical approach to the diagnosis of head and neck tumors diagnostic aids and procedures to be employed and the argument of surgery versus irradiation therapy. In any discussion of radical head and neck surgery the final results as to the benefit to the patient are always to be considered and as the author states "operations on the medically indigent accomplish little in the way of positive results. In the author's presentation of preoperative basic concepts it is obvious that a most intelligent and practical judgment has been used. This is not a basic surgical textbook nor is it intended to be such however the surgical technics that are explained throughout the entire text are most adequately described and shown. The reviewer agrees with the author about the term "recurrence. There is no doubt an entity of recurrent cancer however as he states residual is most often the more correct term and probably is due to the fact that considerable head and neck surgery is done by less fully trained surgeons. This is an excellent presentation of the basic principles of a most highly specialized type of surgery.

—CLINTON S LYTER Col MC USA

**METHODS IN SURGICAL PATHOLOGY** by *Henry A Teloh* M D 127 pages  
Charles C Thomas Publisher Springfield Ill 1957 Price \$4.75

There has been a need for some time for a manual of procedures for describing and processing tissue sent to a laboratory of surgical pathology. This is such a manual and the author and publisher deserve commendation for making it available. It is compact the print is good the few illustrations are clear and in general the contents are adequate. It was written primarily for resident trainees in surgical pathology and it will be very helpful to them. It is recommended for reading by surgeons also particularly the discussions about frozen sections the proper handling of specimens in the operating room and the preferred gross sectioning technic if this is done before specimens are sent to the laboratory. The composition unfortunately is faulty. Awkward sentence construction and frequent and repetitious errors in grammar mar this otherwise worthy effort. The few references to the work of others should be completed.

—WILMOT F PIERCE Capt MC USN

**BODY WATER IN MAN** The Acquisition and Maintenance of the Body Fluid  
by *Arthur B Strauss* M D 86 pages 31 illustration Little Brown  
& Co Boston Mass 1957 Price \$7

The virtue of this book lies not in the revelation of anything new but in the collection of illustrative experiments and their organization into an orderly sequence to develop and verify the current theory of body water and the factors which control it. The chronological historical approach is used both in the introductory chapters tracing the water adaptations of lower animals and within each of the later chapters dealing with specific factors such as thirst renal water excretion

antidiuretic hormone or aldosterone. The references are voluminous and will prove one of the major attractions to a student of the subject.

The scope of the book is broad and of necessity the narration is condensed. In some areas, such as the section on renal excretion of water, this brevity coupled with the special language and symbolism in vogue in this field makes it difficult reading for the uninitiated. It is doubtful if students or physicians not possessing this special background would profit much by it. A major general criticism particularly in the renal section is the failure to clearly differentiate in the experiments quoted between physiologic and unphysiologic conditions and mechanisms. For example, the statement is repeatedly made that drinking of sea water by castaways is not feasible because increased solute load lowers urine concentration and results in greater water loss. The experimental data supporting this conclusion all involve levels of urine flow greater than 5 cc per minute. At the lower rates to be expected of a castaway the relationship does not apply and the conclusion is not justified. In spite of these objections this is a worthwhile book and should be in the libraries of all teaching hospitals and those of individuals with a special interest in the field.

—CHRISTIAN GROVBECK, J. L. C. I. MC USA

THE GLAUCOMAS by H. S. I. S. g. M. D. F. A. C. S. 2d d. t. 516  
p. g. II d. P. ul. B. H. b. In M. d. I. Bo. k. D. pt. f. H. p.  
& B. th. N. w. Y. k. N. Y. 1957 P. \$13.50

This book, which is essential reading for ophthalmologists, expresses the authoritative current opinions on a major ocular problem. The subject is well organized and clearly written. Beginning with a brief historic review, glaucoma is discussed from an anatomical basis to the present broad divisions of narrow and wide angle glaucoma, secondary glaucoma, congenital and infantile glaucoma, and their respective possible etiological factors, pathogenesis, clinical symptomatology, diagnostic means, favored medical therapeutics, and surgical management. The bibliography is noteworthy, and the statistics cited are brief but significant. The preferred surgical procedure representing accredited and responsible consensus is well stated, a feature most valuable but found infrequently in writings on glaucoma. The author has wisely appealed to recognized authorities to incorporate their special contributions, thus further accenting the excellence of the contents. This reviewer enthusiastically endorses the book and extends congratulations to the author. —RUDOLPH P. NADBATH, C. pt. MC USN

CHILD PSYCHIATRY by L. o. Kan. M. D. W. th. p. ef. s. by J. b. C. W. h. t.  
b. m. M. D. Ad. If. M. yer. M. D. LL. D. and Edw. d. A. Park. M. D.  
3d ed. ti. 777 p. g. s. Ch. I. C. Th. m. P. bli. her. Spr. gf. ld. Ill.  
1957 Pnc. \$8.50

The third edition of *Child Psychiatry*, as in the previous editions, covers the field from every practical aspect and with encyclopedic thoroughness. Beginning with a chapter on the history of child psychiatry, the author follows through with basic orientations to include

chronological development intelligence emotional security, personal and parental attitudes and the effect of material environment. He discusses the clinical considerations in the evaluation of the child and the various forms of therapy both pharmacal and psychiatric. The greater portion of the book is devoted to personality problems arising from physical illness psychosomatic problems and those of behavior. There is a short but excellent section on childhood schizophrenia. This book is highly recommended to psychiatrists neurologists pediatricians general practitioners psychologists, and social workers interested in the problems of children and the diagnosis care and management of children with psychiatric conditions.

—STEPHEN MOURAT Lt Col MC USA

**LABORATORY APPLICATIONS IN CLINICAL PEDIATRICS** by Irving J Wolman M D 1 019 pages The Blakiston Division McGraw-Hill Book Co Inc New York N Y 1957 Price \$15

This excellent comprehensive book should be of great value to the medical student entering his clinical years the physician in residency training as well as the general practitioner and pediatrician. It is not an exhaustive text of all detailed laboratory procedures but stresses the intelligent choice and the proper evaluation of results in clinical pediatrics. The author emphasizes that the child is a separate entity from the adult not only clinically but in all aspects of laboratory studies. He points out that with the rapid growth that takes place between birth and early adulthood evaluation of abnormal laboratory findings and the changes in the normal values vary considerably during the progressive phases of growth.

The text is well written and readable. The concise but adequate bibliographies at the end of each chapter enhance the value of the work. This volume fulfills the mission for which it was probably intended namely of being a reference book for handy consultation in a busy office practice or pediatric clinic rather than a formal text.

—JOHN F SHAUL Capt MC USN

**MAY'S MANUAL OF THE DISEASES OF THE EYE** For Students and General Practitioners 22d edition revised and edited by Charles A Perera M D 518 pages 378 illustrations including 32 plates with 93 colored figures The Williams & Wilkins Co Baltimore Md 1957 Price \$6

The twenty second edition of this well known standard textbook as revised and edited by Doctor Perera keeps faith in every detail with the aims that were outlined by Doctor Charles H May when he published the first edition in 1900. It was his aim to present a concise practical and systematic manual on diseases of the eye for the use of the student and the general practitioner. This concept has been adhered to admirably. The familiar format remains the same with 26 chapters and 32 illustrations in colors. Each chapter which deals with a separate part of the eye begins with an excellent review of the anatomy concerned. This is one of the outstanding features of this book. There is no other textbook dealing with diseases of the

eye that adheres so devoutly to the presentation of subject matter without becoming involved in definitive detail. This book is so well known because it is used as a standard text in a great many medical schools that it needs no further recommendations. Suffice it to say that it is a must on every doctor's shelf for ready reference.

—AUBREY L. JENNINGS C I USAF (MC)

MANUAL OF NUTRITION 4th ed. Officially written by G. B. Taintor  
1945 by M. G. Pyke Ph.D. F.R.I.C. 68 p. g. 10 sh. 6d.  
Library Edition New York N.Y. 1957 P. \$3.50

The material in this manual is presented in an elementary form and would be instructive as a beginning text for self study for those who work with food but have no background in chemistry or physiology. Much more information would be gained if the material was presented by an instructor who was well informed in the science of nutrition. The volume contains a brief discussion of classes of nutrient carbohydrates fats proteins inorganic elements and vitamins digestion and absorption energy requirements recommended nutritional allowances food composition meal planning and a very abbreviated table of food composition. Because it was designed primarily to meet the needs of the caterer it is difficult to understand the omission of any reference to the loss of nutrients through improper storage preparation and cooking practices. The essential amino acids are mentioned in the discussion on proteins but no mention is made of the essential fatty acids in the section on fats. Some of the text listed at the end of the manual have appeared in later editions. —ERNEST M. PARROTT Lt C I MSC USAR

SURGERY OF THE BILIARY TRACT PANCREAS & SPLEEN by Ch. I. B. P. Tow M.D. Ph.D. (Surg.) 2d ed. A Handbook of Operative Surgery 381 p. g. 11 x 8 in. by J. W. Phillips Th. Y. B. K. P. B. 1957 P. \$9.75

The second edition of this fine monograph does not represent a major revision of the text. It has been brought up to date however by the addition of newer concepts and procedures and by the deletion of material no longer considered of value. A new section on intravenous cholangiography has been added to emphasize the value of this diagnostic procedure in demonstrating the biliary ducts in cholecystectomized patients. The utilization of body section radiography is included as a technique for sharpening the focus of intravenous cholangiograms by eliminating extraneous shadow. In the discussion of cholecystectomy it is advocated that clamps be placed on the cystic duct and artery a practice which in this reviewer's experience has proved more hazardous than the ligation of these structures in continuity prior to their division. In the section on the pancreas several additional procedures for the surgical treatment of pancreatic disease have been added including the retrograde Roux-Y pancreaticojejunostomy for the relief of chronic pancreatitis as a method of decompressing the obstructed pancreatic duct. Interesting pancreatograms through the distal transected duct are illustrated and tend to confirm the author's belief that the stricture at

the proximal end of the duct often extends from 2 to 5 cm from the ampulla of Vater a situation that would not be relieved by sphincterotomy

One can find in this monograph an excellent description of the standard operations in this field and an ample account of the basic anatomy physiology diagnostic methods and pre and post operative care The line drawings are clear and the index adequate This revised handbook is a fine guide to the education of surgical residents and as a reference work for the practicing surgeon

—JOSEPH J ZUSKA Capt MC USN

**GYNECOLOGIC AND OBSTETRIC PATHOLOGY** With Clinical and Endocrine Relations by the late *Emil Novak* M D and *Edmund R Novak* M D 4th edition 645 pages 683 illustrations 25 in color W B Saunders Co Philadelphia Pa 1958 Price \$14

It is a sad note indeed that this fourth edition will be the last edition of the textbook on gynecologic and obstetric pathology under the name of Novak and Novak due to the demise of the senior author This news however is tempered by the request of the late Doctor Novak that Doctor Donald Woodruff Chief of Gynecological Pathology at Johns Hopkins will collaborate with the junior author in the preparation of future texts on this subject which have been classical contributions to the medical profession

The present text continues the same format as previous ones with additions to the bibliography of the various sections as indicated in bringing the text up to date More thought has been given to the subject of basal cell layer hyperactivity and carcinoma in situ In addition Doctor John K Frost Chief of the Cytology Laboratory at Johns Hopkins Hospital and the University of Maryland is the author of the chapter on recent cytologic developments which is a valuable contribution to this text Exfoliative cytopathology is still in its early developmental stage and not without diagnostic error However it is a tremendous valuable adjunct to other methods of diagnosis and treatment with emphasis toward earlier diagnosis and the important follow up information and other investigative data

The section on breast pathology has been discontinued which is a wise choice in view of recent modern texts delving into this subject alone

Doctor Robert E L Nesbitt has taken the place of Doctor Louis Hellman and has revamped the section dealing with placental abnormalities implantation and placentation There have been changes in some of the illustrations most of which are superior

The medical profession is fortunate in having this valuable text continued by two young specialists in this field who have been inspired by the senior author This is a valuable text for the pathologist and the clinician in this specialty —HUMBERT L RIVA Col MC USA



OPERATIVE OBSTETRICS by R G d D u g l d W l l m B S t r o m m  
 F o r d by N b l o n J E a s t m n. 735 p g l l t r t d A p p l t  
 C t r y-Cr ft I N w Y r k N Y 1957 P \$20

The authors of this text have produced a book of great practical value for every physician who does obstetrics. It is written in a style that makes for easy reading yet is not wordy. Each facet of obstetrics is carefully treated in minute detail complete with etiology incidence complications and therapy as well as expected prognosis. This information is boiled down to usable facts and techniques that are valuable to all concerned from the resident to the fully trained certified specialist in this field. It is also written with such practicability as to be invaluable to the general practitioner who is doing obstetrics. Each chapter is covered with a complete and carefully selected bibliography that makes further reference reading a relatively easy matter.

There is a reasonable amount of detail on each procedure coupled with indications and contraindications of methods and results that may be expected. The latest practice in our outstanding clinics methods of therapy covers all ideas are freely discussed without dogmatism—all of which makes this text very valuable as a reference for a teaching service as well as for an office. The chapter on the use of forceps is worth the price of the text alone. Prenatal preoperative and postoperative care are laid down with a usable clarity that makes the text very valuable. Another helpful chapter devoted to surgery exclusive of the generative tract and a worthy of repeated careful reading by all interested in the obstetrical field. The first 35 pages are devoted to a clear concise review of pelvic anatomy and gives a splendid background for the rest of the book. It is obvious that this work evolved only after years of hard careful study. It is a much needed volume and reflects greatly credit on its authors.

—ROY W TANDY S Capt MC USN

ROOTS OF MODERN PSYCHIATRY by H t r y f P y h t r y by  
 M a r k D A l t s c h u l e M D 185 p g G u n & S t r a t t I n N w Y r k  
 N Y 1957 P 1 \$5.75

Dr Altschule is widely known for his interest in physiologic psychology and especially for his work on carbohydrate metabolism in brain disease. In this book he presents a series of essays on the history of psychiatry since the eighteenth century. At least one of the essays that on Ideas about Anxiety Held by Eighteenth Century British Medical Writers appeared earlier in substantially the same form in the *New England Journal of Medicine* in 1953.

The book is interesting and the author has read extensively in the earlier literature. It is a curious book and in a sense it is history turned upside down. The recurrent thesis of the book is that historical study brings to light earlier criticisms of old ideas that apply perfectly well to the same ideas when they are propounded in modern language and nearly as well to current ideas that are direct outgrowths of those used in the past. This is certainly true provided that one

puts sufficient emphasis on the phrases "the same ideas" nearly as well" and "direct outgrowths" and realizes their limiting significance. The psychiatry of the last two centuries has been predominantly a symbolic and dynamic psychiatry and Altschule sees in its historic "failures" confirmation of its present inadequacy, and a spur to further exploration along physiologic lines.

In the ninth and concluding essay "Greek Revival" Altschule flays Freud and "Freudism" and grossly overstates his case. It is immaterial after all whether the version of the Oedipus legend seized on by Freud is the true legend or merely one of a thousand different versions. One winces at repeated statements of Freud's "slovenly scholarship" and is aghast at the charge of his "poverty of invention." Nevertheless these essays are thoughtful as well as thought-provoking and deserve a wide readership. —FRANK B. ROGERS, LL, Col MC USA

THE MICROBIAL WORLD by Roger Y. Stanier, Michael Duodoroff and Edward A. Adelberg. 682 pages illustrated. Prentice-Hall Inc. Englewood Cliffs, N. J. 1957. Price \$8.

The authors in presenting a modern synthesis of microbiological knowledge in a manner intelligible to the beginner have produced a book which is easily among the best in the field. It should prove profitable to the beginner and instructive to experienced microbiologists. The text includes microbiological methods, microbial anatomy and physiology in considerable detail, the growth and death of bacteria, the major groups of microorganisms, mutation and gene transfer, evolution in bacteria, host-parasite relationships and chemotherapy and the uses of microorganisms. A section entitled "The Biological Background" contains general biological facts considered essential for an appreciation of the study of the microorganisms. Perhaps the chief theme of the book is its emphasis on the role of microorganisms in the enrichment of the study of all living things. The authors excel in pithy expressions and simple but elegant analogies. For example, the meager nutrient requirements of the blue-green algae are epitomized as "pioneers in the biological colonization of the bleakest natural environment." The illustrations are excellent. The discussion of the precipitin reaction, for example, is elucidated by a diagram which shows how an excess of antigen or antibody may prevent the formation of antibody bridges. —LOUIS H. MUSCHEL, MA, MSC USA

EAR, NOSE AND THROAT DYSFUNCTIONS DUE TO DEFICIENCIES AND IMBALANCES by Sam E. Roberts, M.D. With a foreword by Morris Fishbein, M.D. 323 pages illustrated. Charles C. Thomas, Publisher, Springfield, Ill. 1957. Price \$8.50.

The author lists such conditions as hypoglycemic states, vascular headaches, migraine, Meniere's disease, perceptive deafness, Hilger's syndrome, allergies, sinus dysfunctions, and hemorrhagic states in the aged, for which he proposes a system of treatment by correcting various imbalances. The imbalances may be nutritional, electrolytic, hormonal, and acid-base, and insulin-sugar in nature. His basic

therapy consists of dietary correction vitamin and hormone supplementation correction of insulin sugar and acid base imbalances and also supplementation with potassium and calcium and trace minerals without overlooking other accepted therapies. An innovation is the promise by the author to revise certain dietary and instructional cards or charts as new knowledge becomes available bringing the book up to date. Two of these are now available at an additional charge of one dollar and are also convenient to furnish to patients.

There has been a large gap in our knowledge of the medical management of ear nose and throat disturbances which is filled by this book. It could be read with profit by the ophthalmologists and pediatricians as well as by the general practitioners. It is recommended reading for the medical officers and should be used as a reference in our training programs for lectures and for residents.

—LEROY L. KENNEY Captain MC USN

A TEXT BOOK OF X RAY DIAGNOSIS by B t h A th fo lum s  
V l m l 5 p r t C t i N r v S y t m Th T th d J w  
Th Ey Th A ry N l S Th E d T m p l B o e  
Ed t d by S C b a n S h k M D F R C P F F R and  
P t K l e y C V O C B E M D F R C P F F R D M  
R E 3d d t 521 p g 533 il t t W B S und C  
Ph l d l p h P 1957 P \$20

This revised volume of a standard text provides a textbook and guide for those beginning the study of the skull and of neuroradiology. The book does not replace comprehensive reference texts because the authors presume that the reader is familiar with many of the fundamentals of neuroanatomy.

The first two chapters which are concerned with technique and interpretation of plain films of the skull are excellent and place this examination in its proper perspective. The comments on evaluation of suture separation convolutional markings and the pathogenesis of bone changes adjacent to intracranial tumor masses were particularly lucid. The radiographs which accompany the text are in the positive form and are poor in detail and contrast however they are supplemented by line drawings and by clinical photographs which clarify the film reproductions and the text. The chapters on ventriculography and arteriography cover these procedures in much detail including the technique used by the authors. The relative value of air study and arteriography is discussed and much concise clinical data are included.

The technical comments on myelography differ considerably from the standard procedures in American hospitals particularly in regard to the indication for cisternal puncture and to nonwithdrawal of the contrast material after the examination is completed. This textbook is an asset to the radiologist's library and has sections in it of particular value to neurosurgeons and radiology residents. It provides an excellent key to the literature for those interested in further study of neuroradiology. —JOHN A. ISHERWOOD Captain MC USA

THE YEAR BOOK OF RADIOLOGY (1957 1958 Year Book Series) Radiologic Diagnosis edited by *John Floyd Holt M D* and *Fred Jenner Hodges M D* Radiation Therapy edited by *Harold W Jacox M D* and *Morton M Aligerman M D* 445 pages illustrated The Year Book Publishers Inc Chicago Ill 1957 Price \$10

This is an excellent compilation of abstracts of well selected material from the literature for the period June 1956 to June 1957. The abstracts deal with every section of the human anatomy as to diagnosis and radiation therapy. Recent technical developments are mentioned. The editor's introductory comments concerning the controversial subject biologic hazards of diagnostic radiology are well worth consideration.

The book is well indexed for quick referral both as to subject matter and as to authors. It is adequately illustrated. It is highly recommended to all radiologists who are anxious to keep up to date.

—MALCOLM W VASOV Capt MC USN

PSYCHIATRY and the CRIMINAL A Guide to Psychiatric Examinations for the Criminal Courts by *John M. MacDonald M D* 227 pages Charles C Thoma Publisher Springfield Ill 1958 Price \$5.50

This book is an excellent clearly written guide to the major problems of forensic psychiatry involving psychiatric evaluation prior to the institution of or during criminal proceedings. It contains 16 chapters which are short and concise and offer an excellent practical survey of the problem of psychiatry and its relationship to criminal law. The chapters on the simulation of insanity, narcoanalysis and criminal law, amnesia and epilepsy and the electroencephalogram and their relationships to criminal law are particularly good and those chapters dealing with the practical behavior of the psychiatrist as a witness in criminal proceedings are very valuable and can be recommended particularly to the beginner who is new to court procedure.

There is a great deal of factual information in this little book and excellent bibliographies may be found at the end of each chapter. The entire volume can be read in a few hours and it contains sufficient information for most purposes to satisfy the major questions that occur in the psychiatric evaluation of criminals.

Doctor McDonald displays an excellent writing style in this book and very few criticisms can be made concerning the selection of material or his presentation of it. It is the feeling of this reviewer that the second chapter dealing with tests of criminal responsibility could be somewhat longer and more detailed. However taken as a whole one of the outstanding factors of the work is its brevity and conciseness which results in a readable work on a subject which to some people appears dull and uninteresting. Perhaps this book will not have a great appeal to psychiatrists who spend a great deal of time in the court however to the average psychiatrist and student of psychiatry it will prove a very valuable addition to their personal libraries. —ROY F CLAUSEN J Lt Col MC USA

MEDICINE AND THE NAVY 1200 1900 by J J K I I trod ti by S  
H ry Dal Vol m I—1200-1649 255 p g Il tr t d P bl sh d  
by E & S L g t Ltd. Ed burgh nd L do 1957 D t but d  
by Wll m & Wlk C Baltim Md P i \$8 50

This is the first volume of a projected history of medical care in the Royal Navy although attention also is given to general nautical medicine Starting with the Laws of Oleron appr ved in 1194 by Richard the Lionhearted a the legal basis for the treatment of sick nd injured se men the author has carried the story through to the early Stuart period Of no sm ll int rest are the accounts of the houses of pity and other public and church hospitals that cared for not only the s ilor but the poor blind lame sore mī rable sick and impotent people of the land

With abundant references Dr Keevil unfolds the gr du l development of an organized medical service for the king s ships n peace and wa The part played by such men as John Woodall the East India Comp ny the Barber Surgeons Company and other medical groups is carefully described The illust ations are well chosen and definitely add to the interest in the text The book is authoritative and should be of interest not only to every naval surgeon but every naval officer or anyone with a liking for naval history The volume is handsomely and appropri tely bound in navy blue and gold and th typography is excell nt —LOUIS H RODDIS Capt MC USN(R i)

BONE TUMORS G al A pe t nd an An ly f 2 276 C by D d  
C Dahl M D 224 p g Il t t d Ch l C Thom P bl sh  
Sp gf ld Ill 1957 P \$11 50

This excellent book is an analysis of 2 276 cases of bone tumor unselected except for adequacy of material The initial chapter which is introductory and discusses the scope of the tudy is followed by tables classifying the series giving the distribution by histologic type and ge of the patients and the localization of the different tumors The succeed ng chapters discuss a specific tumor except the fin l chapter which is devoted to conditions that commonly simulate pr mary bone tumors The classification is based on that advocated by Lichtenstein

Almo t all of the chapters are identical in arrangement a short generalized discussion being followed by a figure giving skelet l age and sex d strribution of the subject tumor Thi is followed by brief concise informatio under the headings incidence sex age localizat on ympt ms physic l find ngs roentgenologic features gross p thology histopathology t eatment prognosis and bibliography Excellent black and white photog aphs dep ct the x ray and patholog c features of the lesions The book is well bound and printed on glossy paper in large cl ar type The wealth and availability of information and the excellent illustrations make this a highly useful book to those interested in bone tumors —HUGH B HOFFFLER Lt C i MC USA

ANNALS OF THE NEW YORK ACADEMY OF SCIENCES Volume 68 Art  
2 Pages 245 656 October 21 1957 editor-in chief Otto L St White  
lock Subcellular Particles in the Neoplastic Process Consulting  
Editor Cornelius P Rhoads 411 pages illustrated The New York  
Academy of Sciences New York N Y 1957 Price \$5

This paper bound volume is a collection of 28 papers presented at a conference under the auspices and at the New York Academy of Sciences on November 19 and 20 1956 It is a complex detailed and highly technical report of the viral bacteriologic immunologic genetic and pathologic aspects of the etiology of cancer The increasing recognition of the etiologic role of the viruses in neoplastic diseases is emphasized by the attention given to three diseases of virus origin (viral lymphomatosis of the chicken rous sarcoma of the chicken and mammary cancer of mice) An array of data is presented demonstrating the infectiousness and transmissibility of these viruses and the various modifying influences of hormones chemicals and immunizing agents on the host animals Study of this volume is of course a necessity for the investigator in cancer etiology for the clinician a perusal of it can be an inspirational and rewarding experience —ROALD N GRANT Capt MC USN

THE CLOSED TREATMENT OF COMMON FRACTURES by John Chamley  
B Sc M B F R C S 2d edition 259 pages illustrated The  
Williams & Wilkins Co Baltimore Md 1957 Price \$10

In this second extensively revised edition the author has very successfully championed the case for closed treatment of fractures The book is roughly divided into two major portions The initial chapters cover some of the general factors involved in fracture healing and based upon them the author presents mechanical principles necessary for uncomplicated fracture healing He emphasizes throughout the importance of the periosteum and its necessary part in the reduction and subsequent healing The second portion of the book deals with methods of closed reduction and management of specific fractures Nothing is left to the imagination and herein lies the major value of the book Such details as the placement of the operator's and assistant's hands and the utilization throughout the manipulation of forces applied are described and illustrated The pitfalls inherent in each reduction are indicated and the common error of too frequent post reduction plaster changes is noted

This book cannot be considered nor was it meant to be a definitive work on fracture management It is however an excellent supplement to other more comprehensive volumes and will be most useful to the orthopedic and general surgical resident In addition there are many helpful suggestions that will be welcomed by the more experienced fracture surgeon The emphasis on conservative principles the concise descriptions and illustrations of closed manipulative reductions and sound methods of post reduction management all recommend this manual of fracture treatment —STERLING J RITCHEY Col MC USA

CIBA FOUNDATION COLLOQUIA ON ENDOCRINOLOGY V l m 11 HOR  
 MONES IN BLOOD Ed t r for the C b Found t G E W W l t e  
 h l m O B E M A M B B Ch a d E l e C P M l l a r A H  
 W C A R I C 416 pag ill tr t d Littl B w & C B o t o  
 M 1957 Pr \$9

This volume contains the proceedings of the 17th Endocrinological Conference sponsored by the Ciba Foundation. It is devoted primarily to the detection assay and transport of hormones within the blood. The reports dealing with the assay methods for pituitary adrenal and thyroid hormones are concise and well edited. The chapters on hormone transport are enlightening. Though the colloquia is primarily concerned with laboratory techniques and research there are many observations presented which will ultimately be of clinical significance. The participants in the symposium are prominent investigators in endocrinology and the reader will be interested in the discussions which have been presented after each paper. These comments are pertinent and reflect current knowledge and future paths for research in the study of hormones. Research workers and students in the field of endocrinology will find this book of inestimable value. However it offers little for the practitioner.—JOSEPH H AKEROYD Lt Col MC USA

THE DIAGNOSIS AND TREATMENT OF INFECTIONS by D G t j m s  
 M A M D (Cant b) M R C P (L d) 234 p g Chale C  
 Th m s P b l h Sp i g f l d ill 1957 P \$6

This book is an attempt to correlate the clinical and laboratory aspects of present day treatment of infections. It is divided into three parts. The first part discusses current chemotherapeutic agents regarding their antineoplastic range indications for use, their fate in the body and complications resulting therefrom. Part 2 is a discussion of the microorganism responsible for human infections while Part 3 discusses infections of systems.

There is the inevitable overlap inherent in such types of presentation with a little information on certain aspects under discussion followed later by some repetition and more detailed presentation in another section. This requires frequent cross reference and necessitates skipping from section to section for an adequate total picture of the problem at hand.

It was noted in some discussions on therapy of specific diseases that dosage schedules are not entirely in keeping with those recommended by American authors. For example, the intermittent dosage schedule of streptomycin in tuberculosis is not mentioned. It was also apparent in several specific diseases that dosages of drugs are somewhat lower than these generally accepted in this country.

Except as a quick reference regarding the more recent broad spectrum antibiotics relating to their mode of action, range of activity, laboratory data and complications, this book does not fit any special need of the average general practitioner or specialist in this country. It would have limited value for interns.

—JULES J McNERNEY Lt Col MC USA

## New Books Received

Books received by the *U S Armed Forces Medical Journal* are acknowledged in this department. Those of greatest interest will be selected for review in a later issue.

- PEDIATRIC CLINICS OF NORTH AMERICA** February 1958 Symposia on Gynecologic Problems *Goodrich C Schauffler M D* Consulting Editor and Pediatric Ophthalmology *Harold G Scheie M D* Consulting Editor 255 pages illustrated W B Saunders Co Philadelphia Pa. 1958 Price \$15 per year of four numbers (February May August November)
- THE PRACTICE OF INFECTIOUS DISEASE** by *Louis Weinstein Ph D M D* 501 pages Landsberger Medical Books Inc New York N Y Distributed by The Blakiston Division of the McGraw-Hill Book Co New York N Y 1958 Price \$8 50
- A M A SCIENTIFIC EXHIBITS** 1957 sponsored by Council on Scientific Assembly American Medical Association 480 pages illustrated Grune & Stratton Inc New York N Y 1957 Price \$15
- CARDIOVASCULAR COLLAPSE IN THE OPERATING ROOM** by *Herbert E Natorf M D* and *Max S Sadove M D* Foreword by *Warren H Cole M D* 197 pages illustrated J B Lippincott Co Philadelphia Pa 1958 Price \$6
- GENERAL PATHOLOGY** based on Lectures delivered at the Sir William Dunn School of Pathology University of Oxford edited by *Sir Howarth Florey* 2d edition 932 pages illustrated W B Saunders Co Philadelphia Pa 1958 Price \$16
- CLINICAL INTERPRETATION OF LABORATORY TESTS** by *Raymond H Goodale M D* 4th edition 758 page 105 illustrations 6 in color F A Davis Co Philadelphia Pa 1958 Price \$8 75
- PRACTICAL PEDIATRICS** by *R Cannon Eley M D* and *Benjamin Kame M D* 307 pages Landsberger Medical Books Inc Distributed by The Blakiston Division of McGraw Hill Book Co New York N Y 1958 Price \$7
- A THERAPY FOR ANXIETY TENSION REACTIONS** by *Gehard B Haugen M D* *Henry H Dixon M D* and *Herman A Dickel M D* 110 pages The Macmillan Co New York N Y 1958 Price \$3 50
- THE RESPIRATORY MUSCLES AND THE MECHANICS OF BREATHING** by *E J Moan Campbell M D Ph D B Sc (Lond)* *M R C P (Lond)* 131 pages illustrated The Year Book Publishers Inc Chicago Ill 1958 Price \$4 25
- CLINICAL APPLICATIONS OF HYPNOSIS IN DENTISTRY** by *S Irwin Shaw D M D M Ed* 173 pages illustrated W B Saunders Co Philadelphia Pa 1958 Price \$4 50
- COMMUNICABLE DISEASES A Textbook for Nurses** by *Albert G Brown A B M S M D F A C P* the late *Edith B Plant R N* and *John B Craft R N B S M S* 704 pages illustrated edited by *B Saunders Co* Philadelphia Pa 1958 Price \$7 50



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- THE EARLY DIAGNOSIS OF THE ACUTE ABDOMEN by S Za h ry C p  
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- THE YEAR BOOK OF DRUG THERAPY (1957 1958 Y ar B k S ) d t d  
 by H rry B km M D 518 p g ll t t d Th Y ar B k P b-  
 l h I Ch g Ill 1958 P \$7 50
- AIDS TO OPHTHALMOLOGY by P McG M ff tt M D (Lo d ) M R  
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 P r e \$3
- SPINAL ANESTHESIA by J h B D ll B S M S M D Am  
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- CHEMISTRY OF LIPIDES R l t d t ATHEROSCLEROSIS A Sympo um  
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- YOUR CHILD IS WHAT HE EATS A C mm S G d t Child F d g  
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 F R S E 12th ed t V l m 1 G l l t o d t Upp r L mb  
 L w L mb 394 p g ll t t d O f d U v ty P N w  
 Y k N Y 1957 P \$6

# INSTRUCTIONS FOR AUTHORS

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- Fleming A, Young M Y, Suchet J and Rowe A J: *Immunity*  
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*Mycetoma Pedis*

*Studies on Influenza*

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*Propylthiouracil and Thyrotoxicosis*

*Survival after Bilateral Wilms Tumors*

*Prevention of Rheumatic Fever with Penicillin*

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CLINICOPATHOLOGIC CONFERENCE ☆ CASE REPORTS

UNITED STATES

# Medical Journal



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## Foreword

The United States Army Medical Journal is published semi-monthly by the War Department, Office of the Surgeon General, Washington, D. C. It is the official organ of the Army Medical Department and the Army Medical Service. It contains original articles, reports, and news items of interest to the medical profession in the Army. It is published for the Surgeon General by the War Department, Office of the Surgeon General, Washington, D. C. The subscription price is \$5.00 per annum in advance. Single copies are sold at 25 cents. The subscription price for libraries is \$10.00 per annum in advance. The subscription price for the foreign edition is \$15.00 per annum in advance. The subscription price for the foreign edition is \$15.00 per annum in advance. The subscription price for the foreign edition is \$15.00 per annum in advance.

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# UNITED STATES ARMED FORCES MEDICAL JOURNAL

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## JET INJECTION LOCAL ANESTHESIA IN DENTISTRY

A Report of 66 Cases

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EDWARD P. QUARANTILLO *Lieutenant Colonel DC USA*  
ROBERT B. LINDBERG *Lieutenant Colonel MSC USA*

**J**ET INJECTION is the term given to the principle of injecting fluids into the skin and mucous membranes by forcing liquid substances through very small openings or jets at very high pressure. The velocity, depth of penetration and spread depend on the size of the orifice, spring pressure, and type of fluid as well as the type and location of tissue being injected.<sup>1</sup> One of the unique features of this method is the ability of the very fine column of liquid traveling at speeds of approximately 700 feet per second to pierce the tissues without eliciting a pain response or at the most, causing only very slight pain.

In 1947 Hingson and Hughes<sup>1</sup> using jet injection, reported the administration of 0.25 ml of 2 per cent procaine with 1:2,000 epinephrine at a pressure of 3,500 pounds per square inch (p.s.i.) to anesthetize the skin of patients preparatory to performing either caudal or spinal analgesia. In 1951 Krohn, Spriggs and Dabbs<sup>2</sup> injected 29 male patients undergoing anal surgery with 0.2 ml of 4 per cent Xilocaine (brand of lidocaine hydrochloride) in almond oil. Sites of injection were inspected daily throughout their hospital stay and at three weeks after discharge from the hospital. There was no evidence of edema.

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From Research and Development Division, Office of the Surgeon General, Department of the Army.

erythema induration abscess or sloughing. It was shown that these 99 patients exhibited much less postoperative discomfort than a comparable control group.

Hingson<sup>1</sup> reported that on a basis of 5 000 patients he did not believe that inadvertent intravenous injection was as likely with jet injection as it was with the needle and syringe method. He further stated that he was convinced by both clinical and histologic study of tissue that there was less trauma with jet injection than with the needle and syringe.

Although the administration of drugs and local anesthetics by means of jet injection in many areas of the body has been reported in the literature there has been no report of its use in dentistry. The object of this investigation was to determine the feasibility of producing local anesthesia of sufficient depth and duration utilizing the jet injection principle to allow the completion of such routine dental procedures as cavity preparation and the extraction of teeth.

## METHODS

The injectors used were single shot hand operated spring loaded instruments for parenteral injection of medications in calibrated volume of 1 ml or less. They are 21 cm in length and 4 cm in diameter. The jet injector is an interconnected two part mechanism the front part containing the metal ampoule of material to be injected (Metapule) and the back part the power source (fig 1). The only modification of the above instrument for this work was to extend the tip to a length of 2 inches (fig 2).

The power source is a spring activated plunger. On the power stroke the plunger contacts the stopper at the rear of the tetrapule with sufficient force to drive the solution ahead of the loop & through the orifice of the tetrapule.

The injector contains six springs which are energized by compression through a screw and nut principle (fig. 5). The instantaneous release of the spring energy is accomplished by depressing a latch release button.

By reason of high spring pressure and small plunger diameter an instantaneous pressure of 16 000 p.s.i. is developed within the Metapule. As the fluid is expressed from the Metapule, the pressure drops to approximately 7 000 p.s.i. and then tapers off to 3 000 p.s.i. at the end of the shot as the springs expand and lose energy. Due to the nature of the tissue and the second

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ary pressures of 7 000 p s i and 3 000 p s i, the solution is deposited in several layers around the initial channel rather than in a pool as a needle would do, thereby creating a larger surface for greater dispersion of the solution

The solution contained in the Metapule is hermetically sealed in an aluminum container under aseptic conditions (fig 4) The Metapule has in its conical end a minute orifice through which the jet of liquid is expressed (fig 5)

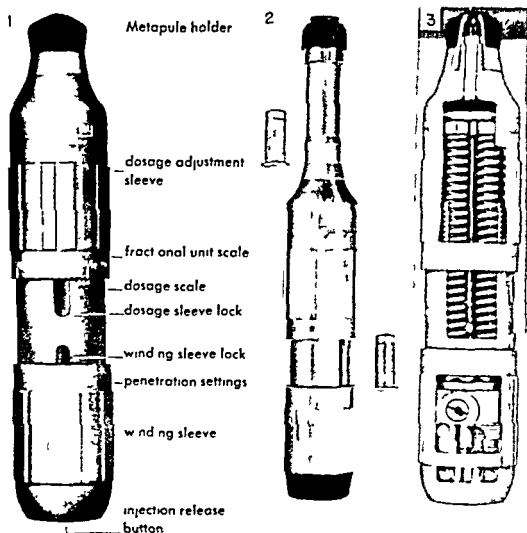


Fig 1 Jet injector for subcutaneous and intramuscular injection of medications and biologicals. Figure 2 Jet injector modified for dental use. Figure 3 Cross section of jet injector showing plunger (top), springs (middle), and needle (bottom).

The injector is made ready for injecting by pressurizing the springs through the turning of a winding sleeve (fig 1) The Metapule is removed from its hermetically sealed container, placed into the front end of the injector. A cap is screwed onto the end of the injector to hold the Metapule in place. The



dosage is selected by use of the rotating dosage scale and the injector is then ready for use

As it is not necessary to touch the sterile Metapule during its removal from the container and placement into the injector it is only necessary to observe the usual technic of preparing the site for injection as is done when using a needle and syringe

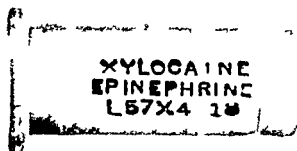


Fig. 4. Aluminum cartridge for Xylocaine Epinephrine

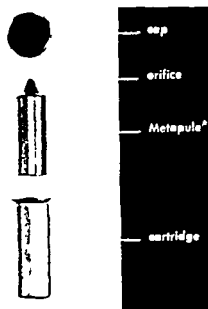


Fig. 5. Exploded Metapule injector components

Because the only injections into mucous membrane previously reported had been in the anal region it was decided to make test injections into the peritoneal and oral tissues of rabbits

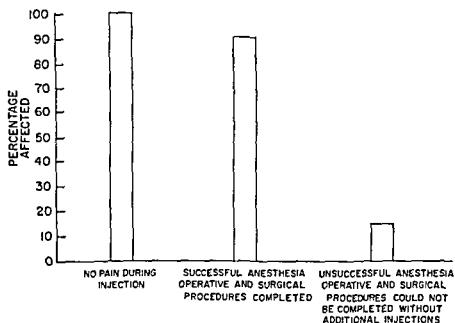
to determine the resistance or nonresistance of those tissues to laceration. It was shown that the tissues were resistant to laceration. To determine the depth of penetration by the column of liquid, methylene blue was added to 0.1 normal saline solution and the series of injections repeated. The animals were killed and examined immediately following the injection and it was found that the depth of penetration was several millimeters. This was considered sufficiently deep to justify the expectation of successful anesthesia in dental use in man.

In all, 66 patients ranging in age from 10 to 37 years were used for this study. Usually only one injection was made per appointment but a number of patients had as many as four injections. The types of injections successfully administered were infiltration, conduction and block anesthesia. Maxillary second and third molars were anesthetized by conduction anesthesia, maxillary centrals through the first molar, by infiltration anesthesia, and mandibular teeth, by use of the intraoral mandibular block and the mental foramen injection as well as the long buccal injection. The operative procedures successfully accomplished were the removal of caries and cavity preparations of all classes in both anterior and posterior teeth in both arches. The surgical procedures successfully completed were the extraction of anterior and posterior teeth in both arches.

The technic of making the injection did not differ greatly from the established techniques using a needle. The same "puncture sites" were used, care being taken that the column of liquid entered at right angles to the area being injected. Any angle less than 90° resulted in a tendency for the column of liquid to make a small clean incision. There was difficulty in administering some of the injections due to the mechanical problem of properly placing the injector tip in the limited space of the oral cavity. The orifice sizes used in this study varied from 0.005 to 0.008 inch. The amount of solution used was 0.6 ml per injection although successful injections were made using 0.3 ml. The anesthetic used was 2 per cent Xylocaine with epinephrine 1:100,000 and 1:50,000. The instrument was disinfected by removing the tip, washing it with soap and hot water, then placing it in benzalkonium chloride.

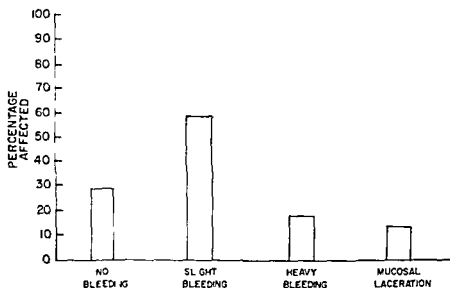
### RESULTS AND DISCUSSION

The most striking finding was that the 66 patients denied any feeling of pain during the injection (fig. 6). This observation agrees with the findings of other investigators that pain was almost totally absent during injection.<sup>1-4</sup> Extraction of teeth, both mandibular and maxillary, and cavity preparation of all classes were successfully accomplished in 87 per cent of the cases (fig. 6). Unsuccessful attempts due to poor anesthesia were recorded in 13 per cent. In this latter group additional



PATIENT REACTION  
(66 PATIENTS)

*Figure 6*



PATIENT REACTION  
(66 PATIENTS)

*Figure 7*

injections had to be made to permit successful completion of the procedure. It should be pointed out, however, that reinjection of patients is required occasionally when using the customary needle and syringe. In 28 per cent no bleeding resulted following injection and in 59 per cent only slight bleeding was apparent (fig. 7). In 13 per cent, however, moderate to heavy bleeding was observed but was controlled easily by holding a 2 by 2 inch sterile gauze pad with pressure over the puncture site for one to two minutes. It was noted that mucosal lacerations were present in the majority of patients in whom bleeding was a problem. The incidence of moderate to heavy bleeding using a needle is negligible.

It was observed further that, in general, the larger the orifice the greater was the tendency for laceration and bleeding. Further studies are needed to confirm this observation. Tenderness at the site of injection, persisting for 24 to 48 hours, was noticed in only a few instances. This occurs occasionally when using the needle and syringe technique. Healing following extractions was uneventful and examination of injection sites for periods extending up to 6 months revealed no abnormalities.

Inasmuch as there is theoretically no penetration of the mucosa by anything other than a sterile column of liquid, the hazard of transmitting infectious hepatitis probably is slight, although further data are required before it may be dismissed. It is further obvious that the danger of needle breakage during injection does not exist.

One might question whether the injection of 0.6 ml of liquid in a fraction of a second would result in a "ballooning" of the area injected. This has not been observed. Figge and Barnett<sup>7</sup> have shown, according to Pascal's law, that a small force amounting only to a few grams, is transmitted to the tissue in contact with the orifice. Preston Goldman, and Thompson<sup>8</sup> reported that a mild degree of tissue distortion occurs in the immediate path of the fluid, but that there was no tissue destruction adjacent to this area. They further reported that repeated efforts were made in dermatopathologic conferences to determine whether the particular skin biopsy specimen under study had been infiltrated by a needle or a jet injector. They found it impossible to differentiate between the two techniques without examining the immediate area. Biopsies done on very fragile lesions showed no distortion of architecture following jet injection into the tissues.

Warren and co-workers reported that in a large series of injections of saline suspended biologicals no apparent trauma was caused. They further stated, "It appears reasonable to state at this time that while considerably more study of jet injection is needed, the procedure will rarely cause undue trauma pro-

vided certain basic precautions are observed. Among these are the use of jets of a diameter of less than 0.008 inch and the proper selection of site and injected material.

#### SUMMARY AND CONCLUSION

It has been shown that dental local anesthesia of sufficient depth and duration to complete successfully routine operative and surgical procedures is feasible utilizing the jet injection principle.

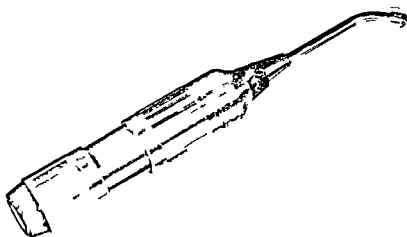


Fig. 8 Jet injector with disposable needle

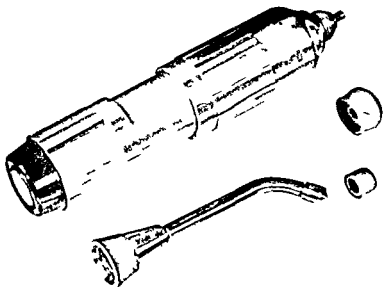


Fig. 9 Jet injector with disposable needle and cap

Jet injection has the following advantages (1) no discernible injection pain, (2) danger of transmitting infectious hepatitis may be less than with the conventional syringe and needle (3) eliminates hazard of needle fracture during injection (4) ease of sterilization (5) the psychic trauma of needle injections is obviated



*Figure 10*

Disadvantages of jet injection are the high incidence of bleeding at the injection site and the cost of the jet injector and the Metapules

These preliminary studies present the first basic change in injection technic in the history of dentistry. The results of this study warrant further investigation to determine the optimal orifice size and spring pressure for a jet injector designed

specifically for use in dentistry. An injector with which these factors could be determined has been designed and is shown in figures 8, 9, and 10.

ACKNOWLEDGMENT The author wishes to thank Robert P. Sheppard and Anthony V. Ditty for their helpful advice.

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# AMPUTATION STUMP PAIN

THOMAS J CANTY *Captain MC USN*  
EUGENE E BLECK *M D*

**T**HE most common complaint of the amputee seeking medical care is stump pain. A review of the Medical histories of over 7,000 amputees treated at this amputation center hospital during the past 12 years revealed that all amputees at one time or another suffer some pain. Not all patients, however, have persistent amputation stump pain.

In a Prosthetic Devices Research Project study at the University of California,<sup>1</sup> it was found that 80 per cent of all amputees were substantially free of pain. Approximately half of the remaining group, that is 10 per cent, experienced incapacitating pain which precluded successful rehabilitation. Experience with a larger number of amputees at this amputation center indicates that 94 per cent of the amputees can be successfully rehabilitated.<sup>2</sup> This implies not only freedom from persistent pain but also ability to carry on with a useful occupation.

The magnitude of pain in individual experiences is related to his so called threshold of pain and to his conception of what constitutes pain. This may vary from a sensation of pressure to one of burning or tingling, and is often described in terms such as "like a hot wire run through the foot," "like a blow from a hammer," or "like a toe being pinched with pliers."

A discussion of the cause of painful amputation stumps may be divided into three general headings: (1) conditions prior to surgery, (2) immediate postoperative pain, and (3) late postoperative pain.

## CONDITIONS PRIOR TO SURGERY

Congenital amputees, as a rule, have little or no pain. On the other hand, a patient who develops gangrene as a result of thromboangitis obliterans may have severe pain that even massive doses of narcotics fail to relieve. Following amputation these patients seem to have more than the usual degree of immediate and late postoperative pain.



Not all gangrene is painful. Gangrene caused by arteriosclerosis may be moderately painful. Gangrene following frostbite usually is mildly painful. Those patients who had major amputations as the result of frostbite incurred in the Korean Conflict suffered less postoperative pain than those whose amputations were the result of severe trauma.

Neoplasm requiring amputation may or may not be painful. If the neoplasm becomes large, severe pain often ensues.

### IMMEDIATE POSTOPERATIVE PAIN

Immediately following operation most amputees experience severe pain from surgical trauma. It is important to realize that postoperative pain following amputation is greater than that following the usual surgical procedures. The pain is more severe because amputation cuts across skin, subcutaneous tissue, fascia, muscle, periosteum, bone, blood vessels, and nerves. Postoperative edema is always present, causing pressure pain. Because the pain following amputation is generally severe, usually large doses of narcotics are indicated for several days. It is rare to find a patient who does not require sedation following a major amputation. After a week or ten days postoperative, most patients require no sedation.

### LATE POSTOPERATIVE PAIN

After a stump heals, the majority of amputees may be subjected to stump pain at intervals for the remainder of their lives. Over 50 per cent of amputees experience stump pain or discomfort sufficient to discontinue temporarily the use of their prosthesis.

About 15 per cent of the amputees have major pain problems that are caused by (1) improper fit and/or alignment of the artificial limb, (2) dermatologic conditions of the stump, (3) bursitis in the amputation stump, (4) osteomyelitis in the stump, (5) trauma, (6) chronic anoxia of the terminal end of the stump, (7) osteoma and/or spurs, (8) neuromata, or (9) phantom limb.

#### Improper Fit and/or Alignment of the Artificial Limb

The time required for a new stump to adjust to an artificial limb is a difficult period. The initial fitting, which amputees undergo, is often a period of severe discomfort and, in some cases, actually painful. Because of the necessity for weight bearing on the stump, this is more marked in a lower extremity amputee. The skin, muscles, and bony prominences, especially over the weight-bearing points of the stump, require hardening and toughening so the amputee can wear the prosthesis without discomfort. The toughening process is exemplified by the irritation of the ischial tuberosity when breaking in an ischial weight-bearing above-knee prosthesis.

There is a common saying among amputees that "the first three years are the hardest." On the average, amputees require a new artificial limb every five years. Most amputees require prosthetic services (alterations and repairs) several times a year. After amputees have become adjusted to their artificial limbs they generally can wear a prosthesis 15 hours a day. Every time an amputee is fitted with a new socket he may again go through this breaking in period. This may be shortened substantially or even entirely eliminated by perfection of fit and alignment of the artificial limb. If the limb is poorly fitted and aligned, the breaking in period is prolonged. If the limb is not in proper alignment, the amputee bears excessive weight on certain parts of the socket, resulting in irritation, discomfort, and pain in the stump. Alignment of the limb must be individually correct for each amputee.

When an amputee begins to use his artificial limb, the muscles which have been atrophied from disuse, and have formed new insertions, also undergo changes that often are painful. It is not uncommon for amputees to develop muscle spasms with cramping pain when they begin to use their artificial limbs.

#### **Dermatologic Conditions of the Stump**

The skin of an amputated stump is subject to disease and conditions that are peculiar to skin as a whole.<sup>2</sup> The skin and the subcutaneous tissues of the stump have not been designed to bear weight and consequently are more vulnerable to the stress and trauma of weight bearing. A factor affecting the vulnerability of the skin to various diseases is that the stump is snugly encased in its socket. Because of misfit of a socket, blisters, ulcerations, and painful calluses are not uncommon on stumps. Furunculosis is not uncommon in a region of pressure on the stump, and a furuncle on the stump is just as painful as one on the neck.

Dermatitis venenata caused by sensitivity of the skin to the material or finish of a socket may occur. Other dermatitides such as psoriasis, lichen planus, pityriasis rosea, or epidermophytosis generally are more violent on the skin of the stump.

As a prophylactic measure amputees are advised to keep their stumps and stump socks meticulously clean. Cleansing the skin daily with a soap containing hexachlorophene decreases the incidence of furunculosis.

#### **Bursitis in the Amputation Stump**

Bursitis may develop over a bony prominence if the protuberance is subjected to undue pressure by the socket. Bursitis over the head of the fibula is a frequent and troublesome occurrence in the below knee amputee. Use of the Navy soft socket aids in preventing this condition.

A painful bursa may develop over the terminal end of a Calander type above knee stump. A bursitis of this type usually can be avoided by complete excision of the bursa about the knee at the time of the amputation. Once bursitis becomes firmly established in a stump surgical excision is the treatment of choice.

### **Osteomyelitis in the Stump**

Chronic osteomyelitis may be a source of continued pain in the amputation stump. The pain may be a sequel to postoperative infections following the initial amputation or it may be caused by pre-existing osteomyelitis in the bone. The principles of treatment in osteomyelitis are the same as those employed in the treatment of bone infection. Systemic chemotherapy alone is usually inadequate but surgery and even re-amputation may be necessary. The severity of the infection, the extent of bone involvement and the resistance to antibiotics indicate the treatment. In general the open flap type of amputation is the safest procedure when osteomyelitis is present.

### **Trauma**

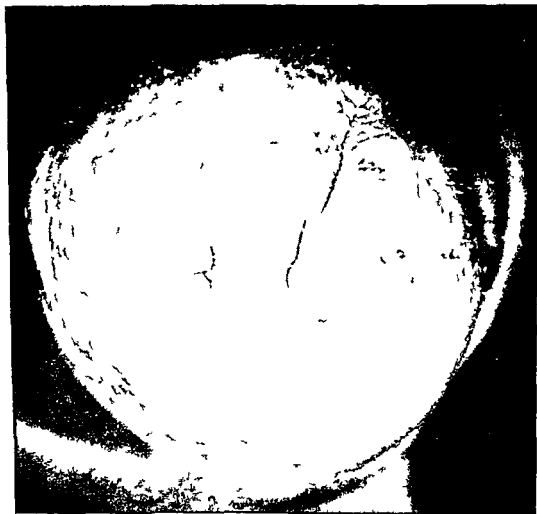
Contusions or bone fracture in the stump may result when an amputee falls. An undisplaced fracture may be treated by application of a compression bandage and rest until resolution has occurred. Displaced fractures require reduction, fixation and immobilization as indicated.

### **Anoxia of the Terminal End of the Stump**

The end of the healed amputation stump is an area where tissue is left with an impaired blood supply. When a portion of the vascular tree is amputated, the smaller remaining blood vessels dilate and carry out the function of supplying blood to the distal tissues. When disease of the vascular tree is present, the terminal tissues have even poorer circulation and the stump readily ulcerates.

For many years amputees have been fitted with open-end stump sockets. The weight bearing points are the lateral walls of the socket, the flare of the bony prominences and heavy tendinous structures. A piston action occurs between the stump and the socket during the walking cycle. There follows slight congestion and edema of the soft tissue on the end of the stump. This swelling is restricted by the lateral wall of the socket so that the only place the stump can swell is at the opening in the bottom of the socket. Chronic passive congestion of the stump end occurs and anoxia of the terminal tissues ensues. Over a long period of time the stump becomes irritated at the distal end leading to *eczema* (fig 1) and at times ulceration. The histologic changes occurring in the skin of the stump have been

described<sup>5</sup> It is not uncommon to find chronic stasis eczema in the end of the stump and occasionally an acute dermatitis may complicate the stasis eczema Not only does pain result, but the patient cannot use his artificial limb Some limb fitters have found that by utilizing a piece of sponge rubber in the end of the socket to act as counterpressure, the chronic eczema can be controlled



*Figure 1 Terminal end of a below-knee stump showing chronic stasis eczema.*

Presently at this center, all stumps are fitted with a closed end socket The socket has a sponge rubber lining which is covered with flexible plastic sheeting (fig 2) We have found that in most patients fitted with the closed end socket, the distal end of the stump maintains a superior state of nutrition and that stasis eczema and edema promptly subside The closed end socket has an accurately fitted wall exerting counterpressure on the entire stump In this way, chronic passive congestion and resulting anoxia are relieved The closed end socket is not a true end bearing socket but is more accurately described as a

total bearing socket meaning that every part of the stump bears its equal share of the weight.

The suction socket with an air space at the bottom of the socket also is helpful in preventing chronic passive congestion of the terminal end of the stump. The skin on the end of the stump is in contact with an air space which has a positive pres

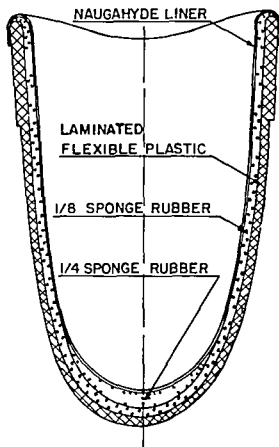


Fig. 2 Detail of the construction of the suction socket.

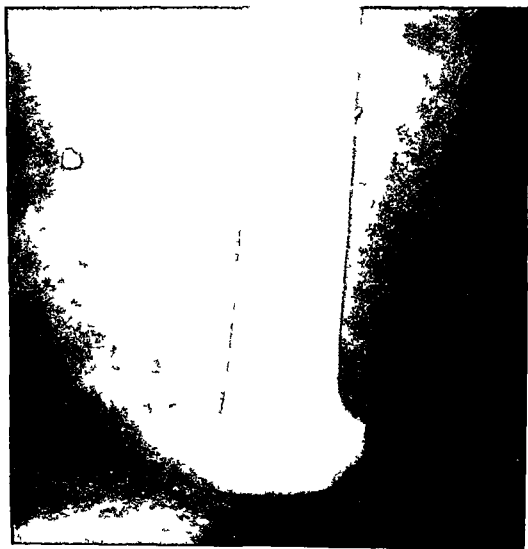
sure of one half pound per square inch. When the amputee lifts his artificial leg during the swing phase of walking the air then changes to a negative pressure of one and one half pounds per square inch. This provides an alternating positive and negative pressure and is in effect a miniature plex boot. Over 80 per cent of the above-knee amputees can successfully wear the suction socket. Unfortunately the suction socket is not without danger because of the critical values of fit and pressure. If the correct fit and pressure are not maintained the suction socket

will cause edema, chronic congestion, anoxia, and ulceration of the stump

Currently at this center an above knee, closed end, soft socket is used which utilizes the suction principle but without a free air space at the bottom of the socket. This new total bearing socket prevents piston action between the socket and the stump and actually locks the stump in contact with the entire inner surface of the socket. The amputee releases the valve to permit removal of the stump from the socket.

#### **Osteoma and/or Spurs**

New bone formation at the amputated ends of bones is not an uncommon finding three to six months after amputation (fig 3). The cause of new bone formation is obscure. It is apparent that some individuals have the tendency to form new bone more readily



*Fig 3 Osteoma at the terminal end of an above-knee amputation three months postoperatively*

than others. Surgical procedures may have some influence on the incidence of osteoma and/or spurs. Ragged edges of periosteum and bone dust resulting during surgery are to be avoided. The surgical procedure employed at this center is to make a sharp incision through the periosteum and then strip the periosteum distally with an osteotome. The bone is sectioned just below the incision through the periosteum. The tissues are then gently lavaged with normal saline solution in order to remove the bone dust.

A bone spur may form if a fragment of periosteum remains in the soft tissue. A spur may be painless but is often extremely painful. It is not uncommon to see a long thin bone spur growing from the end of the sectioned fibula (fig 4). Osteoma may result from an attempt to use a bone graft on the end of the amputated bone. Some surgeons have attempted to place a bone plug in the terminal end of the bone in order to prepare a stump for end bearing. Bone plugs are not necessary. The opened medullary canal of the sectioned bone will heal by forming a smooth rounded table of compact bone in a matter of months postoperatively. An attempt to obtain a bone plug from the shaft of the amputated bone reduces the bone length and naturally produces a shorter stump. It is believed that length should be preserved. A long stump has far greater lever action and longer muscles which permit the prosthesis to be used more satisfactorily. If the bone plug should fail to unite and undergo aseptic necrosis, reamputation results in a shorter stump.

Another cause of bone spur is reattachment of the sectioned muscle to the raw surface of the newly sectioned bone. After amputation the muscle attempts to form a new insertion site. With the constant pull of the muscle on the periosteum where the muscle is attempting to form a new insertion, new bone formation occurs and a spur results. In order to prevent this type of spur formation, the sectioned ends of the muscles are sutured to their antagonists with mattress sutures of chromic catgut. The major muscle groups are sutured to each other, i. e. flexors to extensors. In this way the muscles form their insertions on each other and in the scar tissue of the terminal end of the stump. In addition, by providing anchorage for the sectioned muscles, a stronger and more powerful stump results.

Conservative treatment of painful bone spurs and osteoma consists in providing relief in the socket. If relief cannot be provided, then surgical excision or reamputation is necessary.

#### **Neuromata**

Neuromata are the most common cause of stump pain, but they may cause little or no trouble. All peripheral nerves, upon amputation, heal by the formation of a neuroma at the distal end. If

the neuroma is adherent to raw bone, to the muscle, or to the surgical scar of the skin, it frequently becomes painful. Motion of the stump moves the skin, muscle, and bone. Each time the



*Figure 4 Spur arising from the distal end of the fibula in a below knee amputation*

stump moves, the attached neuroma is stimulated and pain results. This leads to pain in the stump and is often directly associated with phantom pain.



Stone<sup>7</sup> has emphasized that phantom pain is due to the irritation of the nerves and the proper treatment of the nerves at amputation is of prime importance. The procedure of ligating the sectioned nerve ends or injecting them with alcohol at the time of amputation should be condemned. Clinical experience at this center indicates that at the time of amputation the nerve should be forcibly withdrawn distally from its sheath cleanly amputated at the highest level and allowed to retract upward into its sheath. The nerve sheath acts as a protection to the neuroma which develops later. In this way the neuroma cannot attach to scar tissue which in turn is attached to some other tissue in the stump. The neuroma will be well protected high in the stump by the soft tissues and will be within the nerve sheath its natural environment.

Should a painful neuroma be found in a stump the mere excision provides only temporary relief because the new neuroma formed again attaches to scar tissue and the process reoccurs. The resection of the nerve trunk at a higher level likewise provides only temporary relief because a new neuroma forms on the proximal end of the nerve and adheres to the scar and the pain recurs. Some surgeons have reported excising a painful neuroma and implanting the nerve ends into a hole drilled in the bone. This procedure may give temporary relief inasmuch as the portion of the nerve that is buried in the bone atrophies. A neuroma may form at the entrance of the bone where it is sutured to the soft tissues and pain may recur.

Examination of a stump for neuromata should be done with the stump relaxed. On palpating the neuroma the patient will describe sensations along the peripheral distribution of that nerve. It is possible to define the nerve involved from the patient's description of the distribution of pain in the part that has been amputated. Infiltrating the neuroma with procaine hydrochloride may give temporary relief. The treatment of choice is to excise the neuroma, pull down the nerve in its sheath, amputate it at a high level and permit the nerve to retract in its sheath.

#### Phantom Limb

Much discussion has appeared in the medical literature regarding phantom pain. In fact 112 references to phantom limb pain in amputated extremities were found in the literature covering only the past 10 years. Pain itself anywhere in the body is a peculiar type of phenomenon. Although the neuroanatomic pathways of pain have been established, the exact nature of pain and in particular that of phantom pain remains obscure. The University of California's report is an excellent treatise on phantom pain and sensation.

Experience at this center is that all amputees have phantom sensation following amputation. The only exception to this rule has been in those with congenital amputations. It is interesting to note that children before the age of six or seven do not have phantom pain following amputation. After this age, they may develop phantom pain. Because of this phenomenon in children it has been deduced that the body image of self or the "corporal schema" is not developed until age six or seven years.<sup>10</sup>

The usual experience of an amputee is that he has phantom sensation which may be very vivid several weeks after amputation. These sensations gradually fade over a period of one to two years. Most amputees can recall their phantom limb at will for the rest of their lives. Some patients may go for periods of 10 to 15 years and then have a bout of phantom sensation and pain which may last for days or weeks. This latter type of phantom pain is generally from an irritation in the stump. The local irritation can be caused by the reasons previously described. If the cause of irritation is of a permanent nature, little or no relief occurs until the correct treatment is applied. If it is of temporary nature, the phantoms will generally disappear.

Fortunately phantom pain of a major degree exists only in about 2 per cent of amputees treated at this center. Another 10 per cent have temporary bouts of phantom pain which appear for a short period. The patient with constant severe phantom pain has one of the most difficult entities to cure. Reamputation of the stump is generally unsuccessful. Sectioning the nerve above the amputation site generally gives no permanent relief. Choriotomy, sympathectomy, excision of the post central cerebral cortex and even prefrontal lobotomy have a high percentage of failure.<sup>11-14</sup> Many of the amputees who have severe chronic phantom pain become either alcoholics or drug addicts. Very few of these patients are able to wear a prosthesis.

It is believed that phantom sensations and phantom pain are due to an abnormal excitation of the pain pathways involved. The pain pathway is so conditioned that the patient experiences almost constant phantom pain over the terminal distribution of the nerve involved. A strong habit pattern is thus developed. Phantom sensation and pain are often bizarre and phantoms are often misshaped and misplaced along the part of the missing extremity. Patients describe them as having a sensation of the leg being there, or "like a cold rope being drawn between the toes and foot being constricted in a wringer," or "shooting pains in toes, heel, and calf (foot normal length)." It is true that a patient who has severe permanent phantom pain generally develops a psychologic overlay causing additional complications of his condition.

It is believed that the treatment of severe phantom pain or disturbing phantom sensations should be directed toward the cause of irritation of the stump locally.<sup>1-6</sup> Clinical research of this problem lends credence to the idea that peripheal abnormalities located in the stump play a part in the production of the phantom image and pain.

The most common local source of trouble is the painful neuroma. Less common is the ill fitting prosthesis and anoxia of the stump which in turn causes chronic irritation. If the cause is found and the proper relief provided patients with severe phantoms still may experience their phantom pain for a considerable period afterward. The longer the patient has had phantom pain the longer the recovery period will be after the cause has been removed. Due to the firmly established habit pattern even after the cause of the abnormal bombardment of stimuli to the nerve is removed the mechanism for phantom pain through the nerve pathways remains. The only hope for a patient with severe phantom pain is to remove the causative factor and anticipate that with time the conditioned habit pattern of the pain will gradually fade.

Attempts to incite irritations along the nerve segment may change the character of the phantom sensation but generally do not provide permanent relief. Russell and Spalding<sup>1</sup> found that if patients percuss their stumps with a small mallet a temporary relief of phantom pain may be effected. It is believed that the percussion of the stump stimulates a new pathway for pain which becomes greater than the pathway already present. Ultrasonic radiation therapy has not given permanent relief of phantom pain. Some patients have obtained temporary relief by this method.

The treatment of a patient with pain admitted to this center is to carefully evaluate and remove the cause of irritation in the stump.

### SUMMARY

Pain in amputation stumps result from a variety of local causes affecting the stump and each patient must be evaluated individually. Phantom pain and sensation are caused by local irritation in the amputation stump. The proper treatment of amputation stump pain is to remove the cause of irritation in the stump.

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because at distances greater than 1 mile the contribution of neutrons to the total dosage declines rapidly sufficient protection against gamma radiation includes also protection against neutrons. For instance the film material could be divided into two lots and stored in diametrically opposite corners of the basement in order to account for the unknown direction of the expected blast.

A small concrete vault providing some overhead shielding against scattered gamma radiation would provide additional protection. Basement storage proves increasingly safe for bursts at greater distances. If for instance the burst occurs at 2 miles slant distance instead of 1 mile the total initial dosage will be only 1/1000th or in other words ordinary storage in the lower floors of concrete buildings would suffice.

As already mentioned at distances greater than 1 mile the neutron induced activity will be small and readily be attenuated by the protective measures described.

With regard to fallout from an air burst the amount of contamination will be appreciable only in a limited area around ground zero depending on the height of the burst the energy yield and the time elapsed since the explosion. At Hiroshima and Nagasaki for example, the induced radioactivity on the surface was believed to be negligible. At Bikini however where the height of the burst was relatively low the induced gamma radiation from radioactive sodium formed in the water reached two hours after the burst a level of 1 roentgen per hour. This dose rate would suffice to render medical x ray film unusable within 15 minutes. Storage facilities however as mentioned before would suffice for protecting film material even in this case. But such a dose rate would demand evacuation of the area in any case in order to avoid long period accumulation of damaging radiation doses. The local fallout soon after the explosion will be relatively unimportant for air bursts. Over longer periods however, the fallout will extend over larger areas but time for protective measures usually will be available.

### SURFACE BURST

With a surface or subsurface burst the local fallout will assume major significance. Additionally destruction near ground zero will be complete within a wide area thus eliminating all means for medical radiography whether based on the use of photographic material or other recording systems *e g* xerography.

In a surface burst large amounts of debris earth and dust are taken up into the fireball where they are fused or vaporized and become intimately mixed with the fission products. The larger and heavier particles will descend from the column within about an hour and will form a roughly circular pattern around

ground zero. The smaller particles are carried upward and may spread out some distance before they begin to fall. The time taken to reach the earth and the horizontal distance traveled will depend on the height reached, the size, and the wind pattern. Very fine particles may remain suspended for long periods and may travel many thousand miles. Most of the larger particles, however, probably will reach the earth as local fallout within a few hundred miles.

Protection against fallout radiation presents difficult problems because of its widespread and persistent character. The contaminated area can be expected to extend well beyond that in which casualties result from blast, thermal radiation, and the initial nuclear radiation. Protective measures can be classified into passive and active categories. Passive protection implies remaining in the contaminated area and seeking shelter. Even basements of frame houses can attenuate considerable fallout radiation provided that commuting from and into outside areas is avoided. Active protection entails evacuation and/or decontamination. Both procedures inevitably are hazardous because they involve exposure of operating personnel.

Seeking shelter in relatively closed structures may be regarded as the best initial protective step. If commuting to outside areas is kept to a minimum, then the radiation level can be kept very low, and properly stored x-ray film material will hardly be affected. The decay of the fallout radiation with time will rapidly improve the situation, allowing also for improvised protective measures for all photosensitive materials. Continuous monitoring of the radiation level is essential. If film material, stored in the sheltered area at the time of the burst (e.g., in a normal hospital) should become contaminated or exposed to the initial blast, its replacement by new material from an outside source through a contaminated fallout area becomes a problem. It must be transported in vehicles which offer some degree of protection, e.g., by suitable shielding or distance. For instance, if the material is flown into the area by helicopter, both height above ground and reduced time of exposure can keep the radiation level below a damaging threshold even over heavily contaminated areas. Once in the shelter, the film material will be safe.

Two features of fallout radiation are characteristic: (1) its relatively slow build up with time (slow in comparison to the initial burst radiation which is delivered within a few seconds after the blast) and (2) its subsequent decay. Depending on distance and meteorological conditions, evacuation or seeking shelter are the two alternative protective measures. During the build up period a good deal of protective emergency measures in the shelter area can be arranged, particularly if personnel trained for emergency are available. The shelter, of course, must not

be abandoned until the time decay of fallout radiation ensures radiation safety

A short remark may be added with regard to the contamination of water used for processing x ray films. If the water contains radioactive particles they might appear as black spots on the developed films, but only if the particles are present in the developer where the time of contact is restricted to 3 to 5 minutes. In cities where the water from a reservoir is subjected to regular treatment (coagulation, sedimentation and filtration) much of the radioactive material will be removed. Underground sources of water generally will be free from contamination as opposed to rain water which is likely to be heavily contaminated. In cities where the water is taken directly from the river and merely chlorinated it may be unfit for consumption but still be usable for film developing. The provision of a small ion exchange column or water distillation unit for emergency use might be considered. A home water softener would serve the same purpose. Water already in the sheltered area at the time of the explosion *e g* in water heaters will be free of contamination. And even if small black spots due to contaminated processing solution should be visible on the developed radiograph this normally should not be detrimental to its diagnostic value. A repeat radiograph would be helpful in critical cases.

Summarizing it can be said that conventional medical x ray film still would have its place in areas affected by nuclear radiation. This fact is often overlooked. The use of film instead of other recording means remains preferable in view of the fact that the dosage required for a good radiograph is considerably lower for medical x ray film than for any other system known so far, thus avoiding any excess radiation in addition to the level already existing.

For example the dosage required to obtain a deep body radiograph by means of xeroradiography is approximately 5 to 6 times higher than by means of conventional radiography using x ray film.

Consequently the protective measures for storing and handling film are well worth the efforts.

### SUMMARY AND CONCLUSIONS

The sensitivity of medical x ray film in its original container to nuclear radiation is approximately 1/1000th of the sensitivity which the film assumes when exposed to diagnostic x rays when in contact with intensifying screens.

Near ground zero of a nuclear explosion medical x ray film and equipment are rendered useless. However general destruction in this area is so complete that no means for medical radiography would be available regardless what radiographic system would be used.

For distances greater than 1 mile from a nuclear air burst, storage in a basement would provide sufficient protection for medical x ray film from the initial blast

For surface blasts, protection against fallout radiation must be considered in addition to shielding against the initial blast. Basement storage of film material will be adequate in most cases. For transport of film through heavily contaminated areas, monitoring of the dosage to which human life is exposed will indicate the time limit up to which film might be usable.

As an additional precaution, particularly against scattered gamma radiation from the initial blast, two small concrete or brick vaults to be placed in opposite basement corners are recommended for film storage.

The danger of reducing the diagnostic value of a radiograph due to contamination of the developer solution is considered insignificant.

Medical radiography using conventional x ray film will be feasible in the neighborhood of a nuclear explosion without extreme measures for protecting the film.

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#### A NONSMOKER SPEAKS OF SMOKING

Physicians who smoke cannot in honesty recommend no smoking to their adult patients. Not that is unless they preface the warning with that trite phrase "Do as I say, not as I do." The best argument against a physician smoking is that for the most part and for the longest time the odor from his mouth carries the memory of a cuspidor in a saloon. Needless to mention, the writer of these sentences is a nonsmoker from way back, not a Johnny come lately to the abstainer's bench. Don't smoke if you tell your patients not to.

—EDITORIAL  
in *New York State Journal of Medicine*  
p 340 Feb. 1 1957



# MEDICAL ECHOES

WALTER L. BIERRING M D

IT is difficult to select a theme worthy of this occasion yet it may be of interest to recall certain impressions gained during the formative period of a medical life of personalities and epochal events that sound an echo down through the years and thus endeavor to estimate their part on the medicine of this later day

Viewed through the perspective of memory three outstanding personalities—Billroth Pasteur and Osler—left an enduring impress and may form the basis of the thoughts I wish to present

I came into medicine in March 1892 some 65 years ago after the completion of a graded course of six months each with a teaching hospital of 50 beds Yet in this somewhat limited teaching environment were two inspiring spirits that opened up entirely new fields of thought for the inquiring student One was the professor of anatomy later a leading surgeon who had received a medical degree from two universities in this country a member of the Royal College of Surgeons of England with graduate studies during four years in the laboratories and clinics of London Berlin Vienna and Paris including a course in bacteriology at the Royal Institute for Infectious Diseases in Berlin with Professor Robert Koch He brought the first oil immersion lens centrifuge and stomach tube to the Iowa University Medical School besides presenting an unusual course in neuroanatomy and demonstrations in neuropathology

The other was the professor of chemistry who gave the first course in biochemistry at the institution and had spent the last four summer vacation periods in the laboratory of Professor Hoppe Seyler in Strausburg then the leading physiological chemist in Europe

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These two leading scientists inspired the urge for further study—and perhaps you will share with me the thrill of being suddenly transported a few weeks following graduation into the field of opportunity such as was offered by medical Vienna during its so called "Glanz periode "

This famous university medical school with its laboratories in the basic sciences was grouped around the general hospital "Das Allgemeines Krankenhaus" with its 2,600 beds. Within its walls at that time there were over 10,000 births annually, and more than 2,700 deaths. Great names were then a part of Vienna medicine. There was Northnagel, Kraus, Neusser, and Kovacs in internal medicine. Billroth, von Eiselsberg, and Albert in surgery, Lorenz in orthopedic surgery. Chrobak, Schauta, and Braun in obstetrics and gynecology, Frankl-Hochwart and Krafft-Ebing in neurology and psychiatry. Kaposi in dermatology, Kolisko, Weichselbaum, Paltauf, and Gruber in pathology and bacteriology. von Ebner in histology. Obersteiner in neuropathology. Fuchs and Stellwag in ophthalmology. Politzer, Gruber, and Urbantschitsch in otology and Schnitzler, Hajek, and Chiari in rhinolaryngology. Inasmuch as autopsies were the rule, unusual opportunities were offered for the study of gross and microscopic pathology.

It was an era of the therapeutic nihilism when the art of clinical diagnosis reigned supreme with the subsequent autopsy report to confirm or change the clinical conclusions. It was said of Professor Neusser in internal medicine that he sent 100 consecutive clinical diagnoses to the autopsy room without an error.

By a fortunate circumstance I early came to know Assistant Professor Anton von Eiselsberg, and through him came under the influence of his great chief, Professor Christian Albert Theodor Billroth, then recognized as the premiere European surgeon and pioneer in visceral surgery.

In 1892 Billroth was completing 25 years of professorship in the Royal University of Vienna, which occasion led to a wider publication of the various episodes of his eventful career. He was born in Bergen, on the island of Rügen, but received his general and medical education at the universities of Greifswald, Göttingen and Berlin.

At 24 years of age, he became assistant to Professor Langenbeck of Berlin, where he had an excellent opportunity to learn operative surgery. However, his studies on comparative and pathologic histology of the spleen, the structure of lymph nodes, periostitis resorption and normal growth of bone attracted so much attention that in 1858 he was offered the professorship of pathology at the University of Greifswald. This he declined,

but two years later he accepted the chair of surgery at the University of Zurich Switzerland. It was here that he completed his monograph on *Cocco bacterium septica* that presented a true concept of wound infection. While at the University of Zurich the first edition of his *Handbook of Surgical Pathology and Therapy* was published which became so popular because of its pleasing and clear presentation of the various subjects that it required a new edition almost every year. In the introductory chapter he stressed the necessity that The Surgeon should combine general medical knowledge based on capable anatomical and physiological background and a surgeon who is able to do that and has at his command the artistic side of surgery may boast of having attained the highest goal in general medicine.

At the ceremony attending the silver anniversary of Billroth's professorship in Vienna his colleague Professor Albert referred to the Faculty requirements for the professorship of surgery in the Vienna school which included the highest art as a practical surgeon and scientific investigator as well as in physiologic and pathologic research furthermore a teacher operator writer and a pleasing personality. All these were met by Billroth when he answered the call to Vienna at which time he was 38 years of age.

This is all more significant when we consider the period 1867 nine decades ago. In his new field he reached his greatest prominence as a pathfinder when he introduced surgical treatment in gastrointestinal disease. He was also the first to undertake total extirpation of the larynx and the esophagus as well as gastroenterostomy and stomach resection which opened for surgery a wide and productive field. He contributed to practically every field of surgery. I was privileged to be present at several plastic operations on the face by Billroth which were done as carefully and expertly as a pyloric resection or extirpation of the larynx.

I also witnessed in 1892 my first thyroidectomy and removal of the Gasserian ganglion by von Eiselsberg first assistant to Billroth. During that year this brilliant young surgeon reported his interesting researches on hypoparathyroidism in relation to tetany.

Billroth and his pupils Czorny Gussenbauer von Hacker Wolfler Gursun von Mikulicz Radecki von Eiselsberg Salzer and Fraenkel formed a school of surgery that became a nursery of professor as all of the aforementioned became teachers of surgery in leading European universities. Billroth was a monumental figure such a comes but once in a generation from whose presence a light emanates that shines through the years ahead reflected in part by the brilliant achievements of American surgeons in early part of the twentieth century.

Billroth had a gracious manner, spoke a pure German, and was very kind and considerate to American students and physicians. Frequently at the close of a clinic session or ward visit, he would explain certain features of the operations performed and the diagnostic problems involved. His knowledge of physiology and pathology added distinctly to the discussion. Occasionally he would speak of a delightful musicale with his friend Johannes Brahms the evening before. This great composer dedicated to Billroth two of his string quartets. In his letters, *Briefe von Theodor Billroth*, published in 1895, one year after his death, we have a glimpse of his beautiful soul and sterling character, and gain a further realization of his intimate friendship with Brahms, Hanzlick, and other great figures in the field of music, as well as with the leading surgeons of his time.

It was in keeping with the sentimental Viennese to produce a photograph at the ceremony of the 25th anniversary of Billroth's professorship, in September of 1892, which portrays Billroth standing on the veranda of his summer home at St. Gilgen in the Austrian Alps, viewing the beautiful autumn foliage of the surrounding hills, and subscribing his signature with the words of Hebbel, *Dies ist ein Herbsttag wie ich keinen sah*. (This is an autumn day the like of which I never saw.)

The last two decades of the nineteenth century was a period when bacteriology was becoming an integral part of medical and clinical investigation. Two schools of this new science were shaping the current of thought in all fields of medicine, that of Louis Pasteur in Paris and Robert Koch in Berlin.

The teachings of Robert Koch predominated in the German and Austrian schools. His discovery of the tubercle bacillus in 1882, the demonstration of the *Spirillum cholerae asiaticae* two years later as well as the comprehensive studies on the anthrax bacillus had established his fame as a bacteriologist. His introduction of solid culture media had placed all bacteriologic investigations on a firmer foundation.

During the years 1892 and 1893 there had been opportunity for taking short courses in bacteriology with Professor Paul Ernst in Heidelberg and Professor Max von Gruber in Vienna, both former assistants of Professor Robert Koch. The course in Heidelberg was interesting. It was the first formal course attended in the new science. For the first time spores and cilia were successfully stained. The cultures of tubercle bacillus and spirillum of Asiatic cholera used for study were from the original strain first developed by Koch, 10 and 8 years previously. The existing epidemic of cholera in nearby Hamburg added a further interest. For the first time the characteristic rice water intestinal contents were observed.

Pasteur was generally recognized as the father of bacteriology the discoverer of a new world that of the infinitely small His studies in bacteria extended back to 1854 and early recognition that all fermentations were due to micro organisms—the making of wine through fermentation of the grape, the souring of wine to produce vinegar the decomposition of all animal matter by bacteria and the final overthrow of the theory of spontaneous generation

His first studies in disease were with chicken cholera and the demonstration of a small coccobacterium as the causative agent He was able to produce a vaccine through attenuations of cultures grown at a lower temperature than is natural for fowls—which proved very effective as a protective agent

His further epoch making demonstration with protective vaccines in anthrax and blackleg saved the cattle industry in France He was equally successful in controlling the diseases of silkworms where he first recognized the difference in virulence in infective micro-organisms This led rapidly to the study of wound infection

In 1873 came the historic letter to Pasteur from Joseph Lister the surgeon of Edinburgh reporting his first successful results in the use of surgical antiseptics based on the studies of Pasteur

Less than twenty years later in the fall of 1892 these two great leaders met on the stage of the Sorbonne in Paris at the exercises for the celebration of Pasteur's 70th birthday Joseph Lister gave the principal address on this historic occasion

During the eighties had come the remarkable studies in rabies and the development of antirabic protective vaccination

It was the efore one of life's privileges to come to the Pasteur Institute in Paris in the early spring of 1894 then No 25 rue Dutot now renamed "rue le docteur Roux" near the Boulevard Pasteur It is interesting to recall that the laboratory table at the Institute assigned to me had just been vacated by Dr Charles F Martin of Montreal later for many years Professor of Medicine and Dean of the Faculty of Medicine of McGill University

The Pasteur Institute had been built in 1868 by funds collected by popular subscription as an expression of a grateful French people in recognition of Pasteur's scientific discoveries in saving the wine silk and domestic animal industries for France as well as his epoch making contributions to medical science and the control of human diseases

In 1889 Pasteur had transferred the Directorship of the Institute to his pupil and assistant of many years Dr Pierre Paul Emile Roux The associate Directors were Doctors Metchnikoff Borrel Martin Chamberland and Calmette The principal contacts

were with Roux, Metchnikoff, and Borrel, and it may be of interest to record a few impressions retained of each.

Dr Roux had been so closely associated with Pasteur particularly in his early work on anthrax and rabies, that he breathed the very spirit of the Master. He had been the principal assistant of Pasteur during the period of the preventive treatment of rabies. In 1887 he had demonstrated with Yersin the specific toxin of the bacillus of diphtheria and the bacillus of tetanus. Dr Roux was of slender build slightly stooped always wore a black skullcap, had a kindly face, with a distinctly penetrating eye and an inspiring personality. His was a life devoted to science. He had not married and had his living quarters in the Institute; there he also had his last sleep on November 3, 1903, at the age of 80 years. A simple marble tablet in the courtyard of the Institute marks his resting place.

Dr Elie Metchnikoff, the Russian biologist, had been an associate of Pasteur for a number of years, and practically all of his further researches in phagocytosis and immunology were carried on in the Institute. A vivid memory remains of the interesting figure he presented as he walked across the courtyard to and from the animal quarters. I can still see the large head with black beard and long locks of hair, body bent slightly forward, with test tubes of culture media in one hand and glass pipettes in the other and from the side pockets of the long laboratory gown, a number of guinea pigs and white rats sticking out their heads. On one occasion I accompanied him to the animal quarters to obtain saliva from a dog with rabies. The dog was muzzled but snapping his jaws viciously. Dr Metchnikoff used one of the long pipettes prepared in the laboratory, inserted it into the mouth of the dog, and withdrew by sucking sufficient saliva for his purpose, which is an exhibition of rare scientific courage.

Dr Metchnikoff could lecture with equal facility in French, English, and German, as well as in his native Russian language. He died in 1916, and his ashes are kept in an urn placed in the library of the Institute.

Dr A. Borrel, a bacteriologist, was interested at the time in investigating the parasitic origin of cancer and other malignant tumors. The plates and illustrations of pseudoparasites and cell inclusions, accompanying his publications in 1894-1895, resemble much of what was published by later investigators. His conclusions as stated then are interesting: "It is possible that further research will determine that tumors are caused by sporozoa, bacteria or yeasts, and while all these hypotheses are permissible but up to this time such do not appear to be demonstrable." After World War I, Dr Borrel became professor of bacteriology at the University of Strasbourg.

The course in bacteriology at the Pasteur Institute covered a period of from 10 to 12 weeks upon the completion of which the student was permitted to carry on independent studies and investigations. The forenoon was devoted to a lecture demonstration by Roux Metchnikoff, or Borrel and the afternoon to practical exercises pertaining to the topic under consideration for that day. These included classification of bacteria and microorganisms preparation of culture media glass blowing study of microbes of the air water and soil and pathogenic microorganisms culture and staining characteristics inoculation of animals virulence vaccines toxins and antitoxins. It was difficult to absorb all the new knowledge that was presented. The demonstration of filterable and nonfilterable forms of microbial life was demonstrated by the use of the porcelain filter developed by Chamberland. Assistant Director of the Institute. It was the first suggestion that living viruses existed of filtra microscopic size—later demonstrated with the advent of the electron microscope. Practical demonstration was made of the purification of public water supplies by filtration through sandy soil including a visit to the sewers of Paris and the sewage disposal and soil filtration purification plant at Gennevilliers a suburb of Paris. The importance of denitrifying bacteria in the soil in connection with fertilization was recognized. The demonstration by Pasteur of fractional exposure of higher temperature prevented wine from souring and forming vinegar thus the advent of pasteurization.

Opportunity was offered for the study of special forms of infective microorganisms such as the three types of *Bacillus tuberculosis*—avian bovine and human bacillus of glanders bacillus of leprosy organisms causing hog cholera Asiatic cholera actinomycosis Madura foot and relapsing fever malarial parasites coccidiosis of rabbits ringworm (*Trichophyton tonsurans*) favus (*Trichophyton schoenleinii*) as well as the demonstration by Borrel of coccidia like cell inclusions in cancer vaccinia and variola.

Special attention was given to the study of rabies or *la rage* in dogs and rabbits the latter having the paralytic type of the disease when produced experimentally.

It was demonstrated that the rabies virus was contained in the spiral cord and other parts of the central nervous system in animals dying from rabies. An emulsion of sections of such spinal cords was used for inoculating animals such as the rabbit and with each successive inoculation the virulence increased until the animal always died on the sixth day. This became the fixed virus or *v u fixe* of rabies.

Sections of spinal cords with this fixed virus were suspended in flasks, exposed to dehydration with copper sulfate, resulting in a gradual attenuation of the virus, until by the 21st day it had lost most of its virulence. The attenuated form of the rabies virus, or vaccine, formed the basis of protective vaccination in human persons, or dogs, bitten by rabid animals. These vaccinations were carried out in the dispensary of the Pasteur Institute. Similar institutes for this purpose were later established in different parts of the world.

In this year, 1894, under the direction of Dr. Roux, diphtheria antitoxin or antidiphtheritic serum was produced for the first time on a large scale, by the immunization of horses to the toxin of the diphtheria bacillus. The blood serum of such immunized horses was found to have sufficient antitoxic units to be of curative value in the treatment of diphtheria, as well as for the purpose of protective vaccination. The antitoxin units as determined, formed the basis of serum therapy in diphtheria, being a confirmation of the researches of von Behring and Kitasato in Germany of the properties of serum from animals rendered immune against diphtheria and tetanus.

Between February and July of 1894, 300 patients with diphtheria were treated in the nearby Children's Hospital with anti-diphtheria serum as prepared in the Institute, resulting in a remarkable lowering of mortality rate from 51 per cent to around 25 per cent. For purpose of control and comparison a similar number of patients with diphtheria at the L'Hôpital Trousseau were treated by the older methods of therapy, and the comparative results in observing the patients from day to day as well as in the mortality rate were dramatic and left a vivid impression.

Two personal contacts with Pasteur remain vivid in memory. While Pasteur had his residence in the Institute, he was away a great deal, usually at his summer residence near Paris, so that his visits to the laboratory were real events. One of these visits, early in July 1894, was particularly so for the Institute, because on that day Doctor Yersin, a former assistant director, returned from China with organs and tissues showing the pathologic changes of bubonic pest or plague, and pure cultures of bacillus pestis, the specific causative microorganism of this disease, demonstrated independently by Yersin in China and Kitasato in Japan, both being published in 1894.

The entire day was given over to this interesting demonstration. The Master (Pasteur) remained something over an hour, and freely expressed his gratification over the eventful exhibit, yet added with a sigh: *"Mais il y a encore beaucoup à faire"* (But there is still much to do). No doubt there was in the minds of some that day the memory of the Black Death of the 14th century, when



one third of the world's population died of the plague, and the great epidemic of bubonic pest in London in the 17th century

Another eventful day brought the privilege of an extended audience with Pasteur. I accompanied Dr Roux to the Master's rooms on the second floor of the Institute where we found him seated in his chair with his left hand against the side of his face and wearing the round cap seen in a number of his portraits. He spoke in French with a slight hesitancy in speech due to a partial facial paralysis following a cerebral vascular accident in 1868. He expressed a personal interest in my work of the Institute and inquired particularly regarding the progress of bacteriology and medical education in America. He was familiar with the work of Dr Welch in Baltimore for whom he expressed his high regard. Pasteur was especially interested in the development of two of the newer universities that of Leland Stanford in California and the University of Chicago and marveled at the liberal donations made by Senator Stanford and Mr John D Rockefeller for the purpose of higher education. He added this comment: *Ici il faut toujours tirer le diable par la queue* (Here it is always necessary to pull the devil by the tail)

He was assured that it took a certain amount of tail pulling in our country although philanthropists were manifesting increasing interest in assisting educational institutions. He warded off any reference to his personal contributions to the science of bacteriology but expressed his gratification that the Institute was able to offer opportunities for investigators from all parts of the world to continue their studies in the field of bacteriology and infectious diseases. Adieus and kind wishes ended a memorable conference that left an enduring memory.

The health of Pasteur continued to fail the following year and a final cerebral hemorrhage on September 28 1895 quenched forever one of the most brilliant minds ever bestowed on a member of the human race. Of him it may be said that he changed the medical thought of the world and brought forth a new era in medicine which extends down to this modern day. He rests in the Institute. His tomb is regarded as the finest example of Italian mosaic art in existence. At each subsequent visit to the Institute the last four years ago I have paid my silent tribute.

Many American medical leaders of that day had sought further training in European medical centers and coming back with the flavor of an older civilization brought the impact of the laboratory and clinical teaching at the bedside to the door of every institution concerned with the training of physicians.

In the forefront of such leading spirits was Dr William Osler. It is difficult to present a true concept of the inspiring influence

of Osler on the medical student and young physician, as well as his part in the program of medicine of his period. He was a Canadian by birth, fortunate in his early teachers, and a graduate in medicine from McGill University in 1872 at 23 years of age. Instead of settling down in active practice, he followed the urge for further study with the leading physicians of Edinburgh, London, Berlin, Vienna, and Paris. In Berlin, Virchow was in his prime as the foremost pathologist. Langenbeck in surgery, Traube and Frerichs in medicine, and Du Bois Raymond and Helmholtz in physiology and physics. In Vienna, Hebra led in dermatology and Politzer in otology. Osler attended a variety of courses with Braun in obstetrics, all at the Allgemeines Krankenhaus, his purpose being to study general medicine, as it represented British and European medicine of that day. In Paris he came in contact with Marie and Charcot, leading French neurologists.

Upon his return to Montreal in 1874, he practiced medicine for a few months and then was elected Lecturer in the principles of medicine at McGill University. After one year in this position, he was named professor of physiology, in 1876, and pathologist to the Montreal General Hospital, and in 1880 physician to this hospital.

In 1884, after 10 years of teaching at McGill, at 35 years of age he closed his Canadian period to assume the Chair of Clinical Medicine at the University of Pennsylvania to succeed Dr William Pepper who became Professor of Medicine. His teacher and faculty colleague, Dr R. Palmer Howard, stated that McGill lost its "potent ferment" when Osler migrated to Philadelphia. The same year he was elected to the presidency of the Canadian Medical Association and the following year returned from Philadelphia to preside at the annual meeting held at Chatham in Western Ontario.

In 1885 he gave the Goulstonian Lectures on Endocarditis before the Royal College of Physicians in London.

Osler was warmly welcomed by the medical leaders of Philadelphia—Pepper, Tyson, Stille, Silas Weir Mitchell, Samuel David Gross, J. C. Wilson, Horatio C. Wood, Ashurst and others, and soon became a part of medical Philadelphia.

It was a time when medical teaching consisted largely of formal lectures and amphitheater clinic demonstrations of unusual disease conditions. The institution of ward walks and teaching clinical medicine at the bedside was received with enthusiasm by students and particularly, the younger members of the teaching staff.

The wards of old "Blockley" or Philadelphia General Hospital provided an abundance of interesting disease conditions. Instead

of devoting his afternoon as was custom toward developing a private practice Osler spent the time at Blockley hospital to perform postmortems the careful records of which are treasured traditions of this hospital

His interest in the library of the College of Physicians of Philadelphia led to wider use of the same by students and physicians

Then came the call to Baltimore in 1889 to become one of the Big Four —Welch Halstead Kelly and Osler—to develop the school of medicine at Johns Hopkins University on a plane of high standards unique at that time This new environment and association with leading spirits offered unusual opportunities for one of Osler's training and experience to advance medical teaching and practice as well as the highest professional ideals

Here in 1892 Osler was able to complete his first edition of his *Text Book of the Principles and Practice of Medicine* which ushered in a new era in clinical medicine and formed a milestone in the progress of medical knowledge During the succeeding three decades nine revised editions appeared and for those of us who were asked to teach both in pathology and clinical medicine it formed a constant guide through the changing periods of medical practice

Osler's textbook distinctly influenced the progress of medicine in another direction It is related that a distinguished Baptist clergyman who was close to Mr John D Rockefeller read the first edition very carefully and noted the large number of diseases for which there was no specific or definite form of treatment This was called to the attention of Mr Rockefeller resulting in the establishment of the Rockefeller Institute for Medical Research in New York City which distinctly influenced medical investigation throughout the world

During the 20 years of Dr Osler's period in the United States he stimulated many forward movements in medicine As president of the Medical and Chirurgical Society of Maryland corresponding to the State Medical Society and by his frequent participation in the proceedings of the American Medical Association he added interest and distinction to these new professional relationships

He was a potent force in the organization of two medical organizations the Association of American Physicians and the National Tuberculosis Association He was privileged to train a group of young disciples whose teachers investigators and practitioners formed a School of Osler that profoundly influenced medical education and practice in America He introduced several new syndromes of disease that bear his name

Dr Osler had begun to feel the strain of his quadruple life as consulting physician medical teacher reviser of the textbook, and general bibliophile, so that he even talked of retiring. In all his American years, after leaving Canada he had never become a citizen of the United States. At the same time he was proud of his British origin and too much of a lover of culture not to desire permanent contact with the older libraries and museums in which lay the chief food for his imagination.

During the early part of 1904, there were rumors of Dr Osler's being called to Oxford as Regius Professor. While attending the annual meeting of the British Medical Association at Oxford in July 1904 the honorary degree of Doctor of Science was conferred on Dr Osler by the University of Oxford. Shortly afterward came the formal offer by Lord Haldane, Prime Minister (it being a Crown appointment) as Regius Professor of Physic and it was accepted.

Dr Osler's last migration was deferred to May 1905, and during the following winter and spring he was kept busy attending farewell dinners and exercises in his honor. At all there was the warmest expressions of regard and affection from his many American colleagues.

During this period he also gave three valedictory addresses. At a dinner at the Waldorf Astoria Hotel New York City he said:

I have had three ideals: first to do the day's work well and not to borrow about tomorrow; second to act the Golden Rule as far as in me lay towards my professional brethren and towards the patients committed to my care; and third to cultivate such a measure of equanimity as would enable me to bear success with humility, the affection of my friends without pride, and to be ready when the day of sorrow and grief came to meet it with the course befitting a man.

What the future has in store for me I cannot tell—you cannot tell nor do I much care so long as I carry with me as I shall the memory of the past you have given me. Nothing can take that away.

Many honors came to Dr Osler after he came to England including the conferring of the Baronetcy at the Coronation of King George in June 1911; thus he became Sir William Osler. In 1918 he was elected President of the British Classical Association, the first time an English physician was so honored. His presidential address presented in May 1919 was "The Old Humanities and the New Science."

Like many others I early came under the spell of Dr Osler, but did not meet him personally until June 1899 while attending the annual session of the American Medical Association in Columbus, Ohio. During the following six years there followed other meetings—at Atlantic City, Washington, visits to his clinics at Johns Hopkins and to share with his many American

admirers in the general regret of his departure from Baltimore to become Regius Professor at Oxford University

I saw him but once after he went to England in 1905 and that was in July 1919 From some travel notes a few leaves are taken to recall a happy day spent with Sir William Osler at his home in Oxford My traveling companion Colonel Louis A LaGarde Medical Corps United States Army and I arrived at the luncheon hour Lady Osler was at the station with her Franklin car There were two other visitors Colonel and Mrs Richard P Strong in civil life Colonel Strong was Professor of Tropical Medicine at the Harvard Medical School

We were soon at 13 Norham Gardens Dr Osler met us on the veranda with a greeting such as only he could give He may have been Sir William to others but to us he was still the same Dr Osler we knew in the good days before he came to Oxford in 1905

We were aware that the medical world a few weeks before had taken notice of his 70th birthday At a brief and touching ceremony in London on July 11 with Sir Clifford Allbutt presiding two memorial volumes had been presented to Dr Osler Sir Clifford who was Dr Osler's brother Regius Professor (at Cambridge) had spoken of the memorable occasion as One anniversary of many years of supreme service in two kindred nations and for the world and added the first teacher of his day and one of the most interesting and endowed minds and lovable characters in the story of our profession With his more than 80 years Sir Clifford had made jocular reference to his youthful colleague

Colonel LaGarde and I too, could have testified that age had dealt kindly with Osler although he told us of having spent a week in bed after the birthday ceremony in another bout with the pneumonococcus The black mustache had changed to gray but otherwise the last 15 years seemed to have passed unnoticed In the old time twinkle of the eye the winning smile and the elastic boyish activity we saw the Dr Osler his American friends had always known Colonel LaGarde and Sir William were old friends They had been born in the same year so in their greeting there was much banter as to youthful appearance and the like Sir William recalled the interesting work of LaGarde on ballistics and poisoned wounds done in the laboratory of Dr William H Welch in Baltimore 20 years before

In Osler's many inquiries about American colleagues one appreciated how he still entertained the warmest sympathies for America and her institutions associated as they were with some of his happiest memories One of his first questions was How

is my old friend (James T ) Priestley? Tell him I just picked up several fine old works of his ancestor, Joseph Priestley He was interested to learn that the two grandsons of his friend (Joseph B Priestley, M D , now of Des Moines, Iowa, and James T Priestley II, M D , now of the Mayo Clinic, Rochester, Minn ) had entered the University of Pennsylvania, where once their distinguished ancestor was associated with the medical faculty

We marveled at Dr Osler's memory and knowledge of details of the various happenings in medical circles in America He seemed to know so much about old friends and the service that each had rendered during the war period Many had called on him, Oxford had evidently been the mecca for Americans during the previous five years Lady Osler informed us that her maid had kept a record of the visiting Americans to whom tea had been served The number was over 1 600

Two special hospitals for the treatment of cardiovascular diseases and orthopedic conditions had been established in Oxford during the war, and a large number of American medical officers were stationed there from time to time Lady Osler referred to the great pleasure it gave Sir William to have these fine young men about him Many of us remember his particular affection for the younger members of the profession, and the medical officers who were so fortunate in being associated in service with Dr Osler have treasured the memory of that experience

Sir William was looking forward with interest and pleasure to meeting his many American friends the following year in New Orleans at the Annual Session of the American Medical Association

After luncheon we wandered about the beautiful garden and interesting home with its treasure store of books, later, under the guidance of Lady Osler we saw a bit of the University that Oxford means to most of us There is a particular charm about Christ Church Merton, Magdalen, Pembroke Balliol, Queen's, University Oriel and the other colleges that form Oxford University some are mellow with age, while others belong to the newer group, but about all there cluster many interesting traditions of leading personages in English history Lady Osler particularly desired us to visit the Latin Chapel in Christ Church Cathedral where an interesting military wedding had taken place a year before on June 29 1918 Major Reginald Fitz of Boston had married Miss Phoebe Wright of Ottawa, Ontario, Canada each was the child of old friends, and on leave from France at the time Lady Osler told of the bride s being given away by Sir William and of the reception and tea that followed on the terrace at "The Open Arms," the Osler's home at 13 Norham Gardens "That they should have arranged for this wedding,"

said Cushing<sup>1</sup> was not only characteristic of the Oslers but, expressive of the warmth of feeling which England as a whole felt towards America

There was a short visit to the Bodleian Library with hardly more than a glimpse at its literary treasures Dr Osler had been named one of the curators soon after coming to Oxford in 1905 The duties must have been an attractive part of his new environment. Although he had to assume many new obligations during the war period his interests and sympathies continued to be directed to promoting the highest ideals in medicine His deep interest in the purpose of our visit was one example

For a long time the idea had been in the minds of the leading clinicians and medical educators in the United States that the best means to elevate the standards of medical practice was to develop on a national scale a central qualifying board expressive of the highest type of medical training in our country As an outgrowth of this sentiment the National Board of Medical Examiners of the United States was established in 1915

With the close of World War I the time seemed opportune to have a committee of the National Board in the United States make a comparative study of qualifying examinations as conducted by the Royal College of Surgeons the Conjoint Board of England and the Triple Qualification Board of Scotland The further object of the mission was to acquaint the members of these bodies with the aims and purposes of the National Board with a view to bringing about some form of reciprocal understanding between their country and ours in matters of medical education on the basis of the examination conducted by the National Board The committee consisted of Colonel Louis A LaGarde and me Colonel Victor C Vaughan was detained at home because of the death of his son

In previous correspondence Sir William had been most helpful with advice as to the manner of approach and general procedure and on this day he expressed gratification over the favorable impression that our mission had evidently accomplished The committee had decided to include in its report a recommendation that the National Board extend an official invitation for a British commission of three members representing the qualifying bodies of England and Scotland to come to the United States during the following year for a study of our leading medical schools and teaching hospitals and to attend a National Board examination in Philadelphia The advice of Dr Osler was again helpful in selecting the personnel of this proposed commission and with his approval the names of the following men were submitted Sir Humphrey Davy Rolleston of the Royal College of Physicians Sir Holburt J Waring of the Royal College of Surgeons and representing the Conjoint Board of England and Sir

Norman Walker of the Royal College of Physicians Edinburgh, and representing the Triple Qualification Board of Scotland Sir William was most encouraging in his prophesies as to the outcome of these mutual visits. He recognized their far reaching importance, not only in forecasting still further exchange of professional relations between the two English speaking nations but in advancing the higher ideals of world peace and human welfare.

Sir William and Lady Osler were making ready to leave the next day for a holiday on the island of Jersey. It had been a summer of peace and victory celebrations in England but they were looking forward to this first opportunity for real relief from the great strain of the past five years. The war had brought the keenest sorrow to the Osler home in the loss of an only son. This sadness did not find expression in words although it was in the thoughts of all that July day. It was this quiet heroism in the aftermath of the great war reflected in so many English homes that more than all else engendered a stimulating hope for the future of that sturdy race.

The hour had come to say adieu. There was that in the words at parting—"Mighty glad that you boys came out"—and in the final wave of the hand which left a delightful impression of our visit to Oxford to be more treasured with the passage of the years.

Soon after his return late in September to Oxford, he was called in consultation to Glasgow and Edinburgh. Because of the railroad strike he had to return from Newcastle to Oxford in an open car which aggravated his "bronchitis" followed with bronchopneumonia, pleurisy, empyema, myocardial failure and the end came quietly on the afternoon of December 29, 1919. There was but one Osler. He was fortunate to have his Boswell in Harvey Cushing who in the two volume *Life of Sir William Osler*, published in 1925 told a life story unequalled in all of medicine.

The dedication is significant.

To medical students in the hope that something of Osler's spirit may be conveyed to those of a generation that has not known him and particularly to those in America lest it be forgotten who it was that made it possible for them to work at the bedside in the wards.

From this rich heritage of European culture and education which has been reviewed in brief retrospect one may draw a parallel and proper relation to the remarkable evolution in medical education with the corresponding progress in research and medical practice in America since the turn of the century.



It brought a newer concept of the origin of infectious diseases and closer relation of preventive and curative medicine

An eminent American surgeon at that early period a past president of the American Medical Association spoke these words "Prevention runs like a thread of gold through the entire fabric of medicine"

At the opening of the century there comes to mind the heroic figure of Walter Reed and his effective efforts in the control of yellow fever Directly after the Spanish American War yellow jack had again raised its ominous banner on the rampage in Havana with a heavy toll each day of officers and men

A yellow fever commission was organized headed by Major Walter Reed the other members including medical officers Kean James Carroll Jesse W Lazear and Aristide Agramonte The first effort was to confirm the mosquito transmission of the disease first expounded by Dr Carlos Finlay 19 years before Members of the Commission and two volunteers permitted self inoculation by infected mosquitoes or were bitten accidentally and each contracted yellow fever Major Carroll became seriously ill and Major Lazear succumbed to the infection and thus became a martyr to science

Largely due to the careful experiments by Lazear before his death it was learned that *Aedes aegypti* mosquitoes to be infective must sting a yellow fever victim during the first three days of illness and then before it can transmit its deadly load to infect another person the virus must have a chance to ripen within the mosquito's body for at least 12 days

One still gains a thrill in reading a letter written by Reed to his wife on New Year's Eve December 31 1900

Only 10 minutes of the old century remains here I am sitting reading that most wonderful book LaRoche on Yellow Fever written in 1853 47 years later it has been permitted to me and my assistants to lift the impenetrable veil that has surrounded the causation of this most dreadful pest of humanity and to put it on a rational and scientific basis I thank God that it has been accomplished during the latter days of the old Century may its cure be wrought out in the early days of the new

The problem was solved after 8 months of faithful effort and Camp Lazear was disbanded March 1 1901 Armed with this new knowledge Major Gorgas instituted needed sanitary regulations to control the mosquitoes and Havana was freed of its age old scourge in 90 days Later with this and other knowledge Gorgas made the Panama Canal safe for the passage of commerce of the world and the tropics became habitable for the white man Since then yellow fever has been gradually brought under

world control with the possible exception of the jungle areas in South and Central America, where the infected monkey continues to keep it alive

Early in the century eventful discoveries were reported from Germany. In 1905 Schaudinn, a prominent protozoologist in Berlin, announced the discovery of *Spirochaeta pallida* (*Treponema pallidum*) as the causative agent of syphilis and in 1906 the discovery of the Wassermann reaction was announced by Wassermann, Neisser and Bruck. In 1910 Ehrlich, as the result of his outstanding work in the study of the therapeutic effect of arsenical compounds in experimental syphilis, brought forth Salvarsan or 606, which for a generation was the most potent and widely used drug in the treatment of syphilis. Ehrlich thus created a new science, that of chemotherapy.

During the first decade of this period a young investigator, Dr. Howard Taylor Ricketts of Chicago, began to shed new light on the origin and control of that group of infectious diseases which includes Rocky Mountain spotted fever and the several types of typhus fever. He took up the study of Rocky Mountain spotted fever in the spring of 1906 while on an enforced vacation in Montana. Dr. Ricketts promptly found that the disease was communicable to lower animals and that a certain tick which occurred on a large number of animals in those regions could by its bite transmit the disease from the sick to the healthy animal.

These observations opened a new aspect of problems both in the laboratory and the field and after much hard work over a period of three years he came to the conclusion that in man spotted fever depended simply on the accidental bite of an adult tick carrying active virus. The seasonal prevalence was explained in that only adult ticks find their way to man and they occur only in the spring of the year. During the last year of his life he demonstrated the immediate cause of spotted fever as a small bacillus which he found in the blood of patients and in ticks and their eggs.

In recognizing the marked resemblance between Rocky Mountain spotted fever and typhus fever, Dr. Ricketts had become strongly impressed with the thought that the special knowledge and training acquired in this study would prove of great value in the study of typhus fever and its control.

Typhus fever has been one of the great epidemics of the world. Its devastations are recorded "on the dark pages of history, the pages that tell of war, overcrowding, want and misery."

After careful consideration fully aware of the dangers and risks he would run Dr Ricketts decided to take up the study of typhus fever in the City of Mexico and with his volunteer assistant Mr Russell M Wilder a senior medical student began work in December 1909

Before many weeks had passed results of great importance were secured it was found that typhus is different from Rocky Mountain spotted fever although having many points in common that Mexican typhus is communicable to the monkey and that it may be transmitted by an insect (*Pediculus vestimenti*) a species of louse After several months they were able to confirm the discovery of a micro organism a bacillus in the blood of typhus patients and in the insect

While courageously and devotedly pushing this work to completion Dr Ricketts was stricken with typhus and died in Mexico City May 3 1910 Thus a young and noble career of great achievement and of large service to humanity came to a sudden and heroic end and a new name was placed on the martyr roll of science Many of the observations and discoveries in connection with this work of Dr Ricketts had a much wider significance particularly in the control in World War II of typhus fever and that group of infections now termed the rickettsial diseases

During the Spanish American War more soldiers died of typhoid fever than from battle casualties One of the achievements of preventive medicine has been the protective vaccination against typhoid fever largely instituted by Colonel Frederick F Russell of the Army Medical Corps so that in World War I there was not a single case of typhoid fever in the United States Army Since then through protective vaccination typhoid fever has become a rare disease the only problem remaining being the control of the typhoid carrier

Malaria another mosquito born disease has been brought under effective control in the United States during the past half century This has been accomplished largely through elimination of the special mosquito vector (anopheles) by DDT spraying and destroying all pools and stagnant waters which are breeding places of the mosquito While the anopheles mosquito still abounds in certain areas of the United States the insect no longer spreads malaria as readily as formerly because there are fewer infected people and less opportunity for transmitting the disease

However on a world scale malaria control continues to be challenged It is being met by the organized efforts of the World Health Organization and the World Medical Association

In the malarial region of Asia the Near East, and Equatorial Africa the anopheles mosquito will infect several million people each year of which at least one million will die. The effect will not be confined to the areas involved because malaria has a high impact on the world's economy and also is the major cause of poverty and malnutrition.

A new era in American medicine particularly in the treatment of infectious diseases occurred with the introduction of the antibiotics, just preceding World War II. The first group were the sulfonamide drugs originating in Germany but greatly purified by manufacturers in this country, which reduced the mortality from pneumococcal pneumonia and other acute infections due to streptococci and staphylococci to a marked degree.

The second group of antibiotics of which penicillin was the first example were all products of lower micro organisms such as molds fungi and soil bacteria.

The story of penicillin discovered in 1928 by Dr. Alexander Fleming a London pathologist constitutes another romance in medicine. He prepared the material from a common soil mold and after it was identified by the American entomologist Thomas as *Penicillium notatum* he named the product penicillin. The successful isolation and purification of penicillin and the clear cut proof of its antibiotic action and clinical value with assay and unit of dosage was the work of Dr. Howard W. Florey, and Dr. Ernest Boris Chain at Oxford.

The onset of war expedited the development of penicillin and the great need for its mass production was promptly met by enterprising drug manufacturers in this country. The supervision of its production on a large scale and careful distribution to the Armed Forces and especially civilian hospitals were under the direction of a Committee of the National Research Council all of which was indicative of a broadly conceived program of study and critical research that placed our knowledge of penicillin on a sound basis—a sound scientific and clinical basis. It soon came into extensive use in the military hospitals of all the Allied Nations and may well be accredited with a prominent part in winning the last war. Later it became generally available for civilian hospitals in this country and the dramatic results everywhere were in keeping with the high expectations of the earlier studies.

As penicillin was still powerless in certain bacterial infections search for other weapons led to discovery of a number of other antibiotics all of which have been developed in American laboratories. Waksman discovered streptomycin in 1944 and it became an effective remedy in tuberculosis. Chloro

mycetin developed in 1947 by Burkholder in the Detroit laboratories of Parke Davis & Company has been specially effective in typhus and the other rickettsial diseases Benjamin M Duggar and his associates at the Lederle Laboratories in Pearl River N Y discovered tested and produced Aureomycin later Achromycin which has given remarkable results in the treatment of brucellosis amebic dysentery and such virus diseases as atypical pneumonia psittacosis and the rickettsial diseases Terramycin one of the newer antibiotics has proved to have a still broader spectrum of effects among many of the micro organisms in the bacterial viral rickettsial and protozoan groups

While penicillin is extensively used in a large group of infections the two outstanding results are its use in subacute bacterial endocarditis and the venereal diseases Before the introduction of penicillin subacute bacterial endocarditis a prolonged inflammation of the heart valves was invariably fatal By the use of large doses of penicillin a majority of these cases now are cured and it is acknowledged by leading internists that the new treatment of subacute bacterial endocarditis is barring insulin the greatest therapeutic triumph of this century

It has had an equally remarkable therapeutic effect in the treatment of venereal diseases The former methods of treatment required several years for disappearance of symptoms but now with adequate dosage and prompt diagnosis it is possible to render the infected person noninfective after one or two days and a disappearance of all symptoms of the disease within two or three weeks The incidence of congenital syphilis after effective prenatal treatment of the mother has been reduced to a minimum likewise the admission of chronic forms of the disease in mental hospitals has been lowered greatly There is reason to say that syphilis is on the way out and to hope that ere long the curtain will drop on this the darkest shadow in the land

Within recent years protective vaccines such as the Salk vaccine for poliomyelitis and a vaccine for the Asian strain of influenza have been produced Our knowledge of the viruses and virus diseases has been greatly advanced as since the turn of the century has our knowledge of the noninfectious diseases It may well be said that the era of Pasteur is still with us

The closing years of the last century saw a great discovery in physics—a discovery which was to be of incalculable value to medical science—the discovery of x rays by Wilhelm Conrad Röntgen Professor at the Physical Institute of the University

of Würzburg Medicine profited further from other great advances in physical science—particularly the discovery of radium by Pierre and Marie Curie first announced in July 1898

Largely through the experience with scurvy and beriberi attention was directed to indispensable ingredients in the food. In 1912 Casimir Funk published an article on "Etiology of Deficiency Diseases" and proposed the name "Vitamine" for these deficiency substances. Since then a vast literature has appeared with a classification into vitamins A, B<sub>1-12</sub>, C, D, E, and others, each deficiency being connected with a special disease process. Closely connected with these investigations there has developed an increasing knowledge of the internal secretions, their physiologic functions, and relation to definite disease conditions.

*During the third decade of this period two remarkable achievements came in American medicine in the treatment of diabetes mellitus and of pernicious anemia both classified as deficiency diseases.*

The story of the final conquest of diabetes may best illustrate the integration of scientific research along many lines and finally lead to results of greatest practical importance. It may further be compared to a Greek relay race—where each runner lands the torch to the relay and when the final race is won full credit is due to each who kept the light burning all along the way. Extending back over a hundred years it had its beginning in Liebig's laboratory at Giessen and the study of the hydrocarbons, the recognition of the sugar excreted as glucose, the discovery of a special test with a solution of copper sulfate by Fehling, the contributions by Claude Bernard, the great French physiologist on the glycogenic function of the liver, the demonstration of special islets in the pancreas by Langerhans in 1854, the production of experimental diabetes in dogs after removal of the pancreas by von Mering and Minkowski in the eighties, the demonstration in 1904 of special pathologic changes in the islands of Langerhans, by Opie, the American pathologist and crystallized by the naming of the hypothetical as yet undiscovered hormone insulin, in 1913 by Sharpey Shafer, the English physiologist.

Efforts were made by careful investigators to obtain alcoholic and acidulated extracts of the island tissue of the pancreas, and when the same were injected into depancreatized dogs, the glycosuria diminished and the general condition improved. The prize in the race however was reserved for three Canadian physicians Banting, Best, and Macleod of Toronto who in 1922 were able to report the successful clinical use of insulin in patients with diabetes. A number of modifications have since

been made in insulin preparations permitting less frequent administration of the same and the list of permissible diabetic foods has been greatly increased so that the diabetic patient of today has a wide choice of diet and can live a normal life of many years

During the first 25 years of this century the patient with pernicious anemia could look forward to only one termination as patients rarely lived a year after the first symptoms. This disorder of the blood making system in which the red cells are greatly diminished and the maturing factor of the same is deficient has baffled investigators as to its origin and specific treatment ever since it was first recognized by Addison more than 100 years ago. Whipple in 1921 published the results of repeated bleedings of dogs producing a condition of the blood state similar to that observed in the blood of patients with pernicious anemia. He found further that by feeding these anemic dogs certain foods rich in protein such as liver the blood condition rapidly returned to normal. These experiments formed the basis of the contribution of Minot, Murphy, Castle and associates in Boston in establishing the liver treatment of pernicious anemia.

It was evident that the absence of a constituent of normal gastric secretion in pernicious anemia patients interfered with blood formation. This intrinsic factor interacts with some constituent of food (extrinsic factor) to produce an active anti-anemia principle which is stored in the liver. The liver extracts combine with the intrinsic principle and when given at appropriate intervals maintain the blood of the pernicious anemia patient at a normal level. Since this is clearly a deficiency disease it is necessary to continue the liver treatment more or less continuously for many years. In recent years preparations of folic acid and vitamin B have been used with effective results in special types of pernicious anemia.

Since the turn of the century very significant progress has been made in the diagnosis and treatment of cardiovascular diseases. Early in this period appeared the name of a brilliant general practitioner, Dr. James Mackenzie, who distinctly advanced our knowledge of the diseases of the heart and blood vessels during the first three decades of the century. His medical life forms an interesting story. After graduation from the University of Edinburgh and a year as resident in the Royal Infirmary, he entered general practice at Burnley, a factory town in northern England. In the busy life of a general practitioner his keen mind became centered on two definite objects—first the understanding of the mechanism of symptoms and second the understanding of their prognostic significance.

These were the simple resolutions and definite aims which led to the achievements and great success that came to Mackenzie in later years. He began to study the symptoms in every patient and an accident directed his attention and special interest to diseases of the heart and circulation. A woman patient in labor died suddenly of heart failure. This led him to studying the circulatory condition of women, before, during and after pregnancy. He noted particularly pulse irregularities as an abnormal sign, and soon recognized two types—dangerous and not dangerous. He began to make pulse tracings by means of the old Dudgeon's sphygmograph of every patient and endeavored to analyze them. Soon he began the study of the venous pulse in the jugulars, which led to the ink polygraph that bears his name. By this he was able to make simultaneous graphic tracings of the jugular venous pulse, the carotid pulse, and the apex beat of the heart. By many, this discovery is regarded as the greatest contribution that Mackenzie has made to medicine.

He soon noted so called "missed beats" which he explained as pre-ventricular contractions and named them extrasystoles. Among the dangerous forms of irregularities was a type in which the patient usually died in 5 or 6 years, and all seemed to be victims of heart failure, frequently the result of rheumatic fever. In a patient with mitral stenosis and accompanying congestion of the liver he noted in auscultation that the presystolic murmur was absent. The thought came to him that the auricle had stopped beating. He called this "paralysis of the auricle" and the arrhythmia auricular fibrillation. He noted further that digitalis slowed the fibrillation and relieved the decompensation.

His ideas were not readily accepted by leaders of the profession, and his early papers and writings were refused by leading medical journals. In 1902 he published his book, *Study of the Pulse* which gained great favor in Germany and America long before the giants of the English profession would even glance at it.

After a visit by Mackenzie to America and Europe, many leaders came to Burnley, but few of his own country, with the exception of Sir William Osler, Sir Thomas Clifford Allbutt, and Sir Almroth Edward Wright. So this general practitioner decided to go to the giants, and in 1907, at 54 years of age, he moved to London and opened an office in Harley Street. During his first year he saw but few patients and earned only 114 pounds, or about \$500. There were no hospital appointments or opportunities to teach. However, he was not discouraged, and it gave him the time to complete the publication of his great work, *Diseases of the Heart and Blood Vessels* which established him as a cardiologist. This brought about a great awakening among the giants of the English profession. His annual income in



creased to 1 000 pounds sterling he received important hospital appointments was elected to Fellowship in the Royal College of Physicians of London and the Royal Society of Medicine then elevated to knighthood

He was referred to as a wizard which he resented because he considered that his ability to diagnose and prognosticate was due to knowledge of essential symptoms and warned That no instrument stethoscope, polygraph or electrocardiograph could replace mind and reasoning power of the doctor himself

In 1903, Einthoven of Leyden introduced the string galvanometer now known as the electrocardiograph to the scientific world Mackenzie was never very enthusiastic about it but he was greatly interested in the studies of his distinguished pupil Sir Thomas Lewis who first introduced the electrocardiograph into hospital service in London in 1906 However the electrocardiograph helped to establish Mackenzie as a wizard as it proved his tracings and interpretations to be correct

At the close of World War I in which he served as special consultant in chest diseases he left his consulting room in Harley Street and an income of more than 8 000 pounds a year at 65 years of age to return to general practice in the old university town of St Andrews Scotland a short distance from his native Perth in order to better study the earliest symptoms of disease the significance of the same and the mechanisms of its production On a personal visit a few years later I asked Sir James why he had selected St Andrews and he answered I wanted to practice in a community where 95 per cent of the people were born lived and died there "

In 1919 he established the St Andrews Institute for Clinical Research and here in the wards of the adjoining Andrews College Hospital began the study of the early signs of disease at all ages In July 1922 I was privileged to visit Sir James at St Andrews and had the opportunity to attend the weekly outpatient clinics where the patients were brought in by the practitioners of the town it was easy to recognize the stimulating influence of these conferences on the medical practice of the community As I stood in the long consulting room after a visit throughout the Institute I felt that it all accorded so well with the mind and spirit of the man who acted as my guide

In one of the clinical discussions the subject of hypertension was brought up—and suddenly Sir James grasped the lapel of my coat and said I say Doctor you are going crazy in your country on blood pressure—and you don't know a dum thing about it now do you ? Here 35 years later hypertension is still a problem unsolved

Two years later, attacks of severe angina gradually made it necessary for Sir James to give up professional work and his death came on January 25, 1925. His distinguished disciple, Sir Thomas Lewis, said in tribute, "The greatest of his work lay in the fact that he so developed and simplified the method of approach as to bring it within the scope of the general practitioner."

The classic contribution of Dr James B Herrick in 1912 defined coronary thrombosis as a clinical entity, which was readily recognized by its symptom complex, frequency amenable to therapy and recovery. Dr Fred Smith, an associate of Dr Herrick, by ligation of the coronary artery in dogs produced experimental coronary thrombosis and resulting myocardial infarction, as shown in electrocardiograms. Herrick, with other American clinicians, added a new chapter in internal medicine and distinctly advanced our knowledge of myocardial infarction and degenerative heart disease.

The judicious use of anticoagulant drugs such as dicumarol and heparin has distinctly changed the course of illness in coronary heart disease, as well as the extent of damage to the heart muscle. With the better control of syphilitic infection this form of heart disease has become much less frequent.

It is hoped that the several protective measures instituted to control rheumatic fever, will distinctly lower the incidence of rheumatic heart diseases. Congenital heart disease is now being successfully treated by the surgeon.

The increasing recognition and incidence of coronary heart disease has stimulated intensive research in the genesis of atherosclerosis as it occurs in the coronary, as well as the renal, cerebral and peripheral arteries. It has successfully been produced experimentally in rabbits and chickens by the use of cholesterol or certain food substances with high cholesterol content. In consequence there is a growing concept that the fat content of the average present-day diet is a significant factor in the cause of human atherosclerosis.

Recently a group of cardiologists<sup>4</sup> summarized and evaluated the evidence with the conclusion that, "To date there is no incontrovertible evidence for such a relationship, nevertheless, a strong case is developing to suggest that the nutritional status of an individual is an important environmental factor in the etiology of this disorder. The total fat and the type of fat in the diet are among the nutritional factors particularly involved."

Great milestones have marked the evolution of American surgery during the past half century, too numerous and complex to outline fully. Thoracic surgery, or surgery of the chest, came

into prominence early in the third decade. The successful removal of large numbers of foreign bodies from the heart cavities during World War II developed a technic and experience that led to still greater extension of cardiovascular surgery following the war.

The congenital malformations of the heart and larger blood vessels are now effectively relieved by open heart surgery. Great progress has been made in the surgical relief of chronic defects of heart valves—as mitral stenosis—accompanying rheumatic heart disease. The operation of valvotomy is now well established with remarkable restoration of physiologic function—patients being rendered more comfortable, free from distress, and often able to return to work. Remarkable results also have been obtained in the use of arterial grafts in aneurysm and other forms of arterial disease.

The most exciting recent development in American medicine was the announcement nine years ago by Hench, Kendall, and Reichstein of the discovery of a new hormone of the adrenal cortex called cortisone or compound E, and of a pituitary adrenocorticotrophic hormone (ACTH) and their dramatic effect in the treatment of rheumatoid arthritis. They have been equally effective in the allied group of disorders, the so-called collagen or connective tissue diseases, which include rheumatic fever, *periarteritis nodosa*, *scleroderma*, and *lupus erythematosus*. They present a new therapeutic approach in that the pathologic physiology of this group of diseases is rendered potentially reversible, and have further demonstrated the importance of the adrenal cortex in body metabolism. With the introduction of newer steroids and as the tolerance dosage becomes better established with a clearer understanding of its therapeutic limitations, the future of these new remedies is most promising.

We have all been impressed by the interesting work of Dr. Hans Selye of Montreal in the physiology and pathology of exposure to stress. The concept of a general adaptation syndrome and resulting diseases of adaptation will direct our thinking of disease conditions incident to living in this strenuous age.

In reviewing these epochal events in American medicine, it will be evident that medical education, in order to keep in tune with new discoveries and changes in medical practice, must have undergone an equally remarkable evolution in methods of training during the past half century. One can look back now and see the great drama that took place in medical education in America. Within a comparatively few years the number of commercial medical schools was strikingly reduced, university medical schools were organized, the length of the medical course was markedly increased, the number of medical students dimin-

ished, and there began that evolution that has advanced medical education in America so that it is the peer of that of any country in the world. It must ever be to the credit of the American physician, acting through the American Medical Association, who saw the need of using the constantly growing knowledge and was willing to make the sacrifices that go with change.

There was further supervision of the phenomenal expansion of graduate teaching in medicine. Now, practically all medical graduates have at least a year's internship and hospital residencies have steadily increased with the establishment of certifying boards in the different medical and surgical specialties. These, with fellowships in the different fields of clinical medicine have offered increasing opportunity for training and teaching.

So rapid were the developments in the practice of medicine itself, that it speedily branched off into specialties. One after another they flared on the horizon, some born overnight, self-styled or self-anointed as it were, but these, too, have been brought under supervisory control by the organization during 1933-1934 of the Advisory Board for Medical Specialties, which determines the formation of new boards of certification and, in co-operation with the Council on Medical Education and Hospitals, American Medical Association, gives approval to the residency and graduate training required for certification by the individual specialty boards.

The remarkable discoveries and achievements of American medicine during this period are largely due to physicians and surgeons adequately trained in special fields of research or practice. For a while, with the growth of specialism it seemed as if the family physician of the past was doomed, but gradually the training of the specialist has been pushed up into the hospital years and the undergraduate curriculum in our medical schools is now being arranged to provide a broad well-rounded training for the "basic" doctor who with additional graduate experience will emerge as the general medical consultant of the future, the cultured family physician who will best be able to determine when specialized skill and knowledge is needed for the welfare of the patient.

Because of world wide changes, it must be evident to all that the challenge and responsibility for the future progress of world medicine rests largely with the medical schools, research institutions, clinicians, practitioners, and public health workers here in America. However, if this high place in world medicine is to be maintained it is timely to recognize that American medicine in the future will require the recruitment of superior students, the organization and integration of the community to

supply the opportunities of advanced medical education and continued generous financial support

It has been well said that the past is but a prologue of the future. There are still many unsolved problems in medicine. In a recent two-volume publication by the American Foundation entitled *Medical Research A Midcentury Survey* the following unsolved clinical problems in biologic perspective are listed: cancer, infertility, atherosclerosis, hypertension, rheumatic syndrome, tuberculosis, nature of viruses and virus diseases, alcoholism, and the biology of schizophrenia and human behavior. The continuing increase of an aging population and greater incidence of chronic or long term diseases is profoundly influencing the character of medical practice. The newer fields of aviation and atomic medicine present a further challenge to the medical student, research worker, and practitioner of tomorrow.

With a due appreciation of the great heritage of service and opportunity that we now enjoy, we pray for that wisdom broad and deep to guide aright the destiny of medicine in the days ahead.

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# PROPOSAL FOR A CERTIFIED STANDARD FOR USE IN HEMOGLOBINOMETRY

## Second and Final Report

R. KEITH CANNAN, D.Sc.

IN 1953 the Hematology Study Section of the National Institutes of Health requested the Division of Medical Sciences of the National Academy of Sciences—National Research Council to explore the possibility of establishing a hemoglobin standard for general use throughout the country. In response to this request, the Division in 1954 organized an Ad Hoc Panel for the Establishment of a Hemoglobin Standard under its Subcommittee on Blood and Related Problems.

Dr. George E. Cartwright, School of Medicine of the University of Utah, Salt Lake City, Utah, accepted the Chairmanship of the Panel. Its members were Dr. David L. Drabkin, University of Pennsylvania Graduate School of Medicine, Philadelphia, Pa.; Lt. Col. William H. Crosby, Walter Reed Army Institute of Research, Washington, D.C.; Dr. George Brecher, National Institutes of Health, Bethesda, Md.; Dr. Wallace R. Brode,\* National Bureau of Standards, Washington, D.C.; Dr. Israel Davidsohn, Mount Sinai Hospital, Chicago, Ill., representing both the College of American Pathologists and the American Society of Clinical Pathologists, and Dr. Abram H. Neufeld, representing the National Research Council of Canada. In 1956 Mr. John H. Gould, National Bureau of Standards, succeeded Dr. Brode, and in May, 1957, Dr. Bradley E. Copeland, New England Deaconess Hospital, Boston, Mass., and Dr. Donald E. Brown of the Hackensack Hospital Association, Hackensack, N.J., succeeded Dr. Davidsohn as representatives of the College of American Pathologists and the American Society of Clinical Pathologists, respectively. The Panel also was fortunate in having the cooperation of Dr. Earl J. King of the University of London, Postgraduate Medical School, London, England, who has given his full support to this undertaking.

\*From the Division of Medical Sciences, National Academy of Sciences—National Research Council, Washington, D.C. This study was supported by grant from the National Heart Institute, National Institutes of Health, Bethesda, Md. Contract Number H 2145.

Dr. Brode is now Secretary to the Secretary of State.

Most routine methods of clinical hemoglobinometry depend upon the photometric measurement of a blood sample after quantitative conversion of the hemoglobin which it contains into one or another of its derivatives. For the standardization of such a procedure there is needed a color standard which when measured in the photometer and cuvette in routine use will establish the relation between instrument reading and concentration of the particular hemoglobin derivative. This relation then can be used in converting instrument readings for unknown samples of blood to concentration of hemoglobin by the use of Beer's law or by construction of a calibration curve.

The problem however is complicated by the fact that several methods of analysis involving conversion to different forms of hemoglobin are in common use. Each of these methods should have its own standard. Because a multiplicity of standards is neither desirable nor practicable the Panel decided early in its deliberations to select only one method of analysis for which a suitable direct standard would be developed. It should be pointed out however that this procedure does not preclude the use of the standard for the indirect calibration of another method. All that need be done is to construct a calibration curve based on the measurement of a small series of *normal* blood samples by the standardized method and also by the method which the analyst prefers to adopt for routine use.

In the opinion of the Panel the most significant contribution which could be made to the refinement of clinical hemoglobinometry would be the widespread adoption of a single method of analysis. Failing this the indirect calibration of other methods with the chosen method offers the only simple photometric means for the comparison of data. The procedure however is subject to error if the blood sample contains significant amounts of certain of the abnormal forms of hemoglobin. For example methemoglobin and carbon monoxidehemoglobin are convertible quantitatively to cyanmethemoglobin but not to oxyhemoglobin.

The Panel reviewed the several photometric methods in current use and came to the conclusion that the procedure involving the measurement of hemoglobin as cyanmethemoglobin was the most promising. It offered the following advantages:

1. A simple and accurate procedure has been devised by Drabkin and Austin involving the addition of a single reagent to the sample of blood.

2. The method has been adopted by the U. S. Army after extensive field trials.

3. All forms of hemoglobin likely to occur in circulating blood with the exception of sulfhemoglobin are determined by the method.

4 The color is suitable for measurement in filter type photometers as well as in narrow band spectrophotometers because its absorption band in the region of  $540\text{ m}\mu$  is broad and relatively flat, and

5 The U S Army has had extensive experience in the use of solutions of cyanmethemoglobin as direct standards and has found these to be satisfactory.<sup>3</sup> The U S Army standards have remained unchanged in optical density for extended periods when stored at refrigerator temperatures, provided bacterial contamination was avoided

On the basis of this evidence, the Panel decided to develop a certified solution of cyanmethemoglobin as a standard, and to promote an extensive field trial of its suitability.\* A preliminary report of its recommendations and plans<sup>4</sup> appeared in a number of scientific and technical journals in 1955. This report outlined recommendations of the Panel, described arrangements for the preparation and distribution of certified standard solutions of cyanmethemoglobin, and invited cooperation in an extensive field trial of the use of the standards and of the recommended method of analysis.

More than a thousand laboratories volunteered to cooperate in the trial sponsored by the National Research Council. Distribution of the standards was made with the assistance of the College of American Pathologists, the National Association of Clinical Laboratories,\* the Walter Reed Army Institute of Research, and the National Research Council of Canada. The laboratories not only received descriptions of the procedures for the use of the standards to calibrate photometers, but also directions for the routine determination of hemoglobin in the form of cyanmethemoglobin.

The results of the study were most gratifying. The need for, and the ready and grateful acceptance of, a simple method for the standardization of hemoglobinometers was apparent. The recommended method of analysis likewise was well received. At the onset of the field trial study only seven per cent of the co-operating laboratories had been determining hemoglobin as

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cyanmethemoglobin. At the time of the last report two thirds of the co operating laboratories were using this method.

In the first field trial the standard solutions were prepared from crystalline hemoglobin by Dr David Drabkin. Three solutions in carefully determined concentrations of approximately 60, 40 and 20 mg of hemoglobin per 100 ml were distributed. The optical densities of the final solutions were confirmed independently and a continuing control on stability was maintained in the laboratories of Dr Brecher, Mr Gould, Col Crosby, Dr King and Dr Neufeld. Agreement having been reached on the optical density values, the hemoglobin concentrations of the standards in mg per cent were computed from the optical densities assuming that the extinction coefficient of cyanmethemoglobin per milligram atom of iron (55.85 mg) per liter is 11.5 and that the pigment contains 0.35 per cent of iron.

Two problems were encountered during the course of the field trial study. The first of these was the growth of certain micro organisms observed in some samples in spite of the presence of cyanide. This made it necessary to prepare and to maintain the solutions under sterile conditions. The second problem was a change unpredictable in degree and not reported by all checking laboratories of two to six per cent in the optical density six to nine months after distribution of the standard. Samples from each lot were found to have undergone varying degrees of change, mostly fading, which was compensated in some samples by a comparable increase in turbidity. The standards prepared and distributed by the U S Army in its earlier field trial had remained unchanged in optical density for three years. Inasmuch as these solutions had been prepared directly from whole blood or from washed red cells, it was suspected that the manipulation involved in the preparation of the crystalline hemoglobin for the National Research Council standards might have reduced the stability of the pigment. Therefore a new standard was prepared from washed cells. The new standard was modified further by increasing the concentration of cyanide, both because some previous preparations with such higher concentrations had shown greater stability and because the growth of most organisms would be limited by the higher concentration of cyanide.

Because the percentage change in optical density of the first standard was greater with increasing dilution of the hemoglobin pigment and because cyanmethemoglobin solutions follow Beer's law, the second standard was distributed in only the most concentrated (60 mg per cent of hemoglobin) of the three dilutions.

The second group of standards, modified as outlined above, was distributed in July and August of 1956. Their stability was determined in the laboratories of Dr Drabkin, Dr Brecher, Mr

Gould, and Col Crosby. The stability was satisfactory for at least nine months from the time of preparation, no change of more than two per cent in optical density being observed.

The members of the Panel have concluded that solutions of cyanmethemoglobin, when prepared, calibrated and handled properly, are acceptable as standards for hemoglobinometry. They recognize that such standards are not ideal in all respects. Until better standards can be developed, however, they are of the opinion that the availability of this reagent will simplify greatly the calibration of hemoglobinometers and will increase greatly the accuracy of hemoglobinometry over previously employed practices.

Finally, they encourage further independent investigation in the hope that an even better standard may be developed, particularly one with improved stability and more certain maintenance of sterility.

The National Research Council supplies of the standard cyanmethemoglobin solution are now exhausted and no further production is planned under the auspices of the Academy-Research Council. However, standards are now available from several commercial sources. The NAS-NRC has recommended the establishment of a program of certification of commercially produced cyanmethemoglobin standards to determine conformance with the specifications it has established. In response to the need for the establishment of such a program, as defined by the NAS-NRC, the College of American Pathologists\* has arranged for certification through the facilities of the laboratory of the American Medical Association in Chicago. On the basis of data obtained through this laboratory, the College of American Pathologists will certify whether commercially produced standards which have been submitted comply with the specifications established by the NAS-NRC. *All users are urged to insist that the cyanmethemoglobin standards they purchase commercially carry the certification label of the College \*\**

Detailed instructions for the preparation of the standards have been published by Crosby.\* Producers of the standard or instrument manufacturers may obtain technical details on the adaptation to and use of the standard in the various hemoglobinometers by writing to the Division of Medical Sciences of the National Research Council.

The final recommendations of the National Research Council Ad Hoc Panel on the Establishment of a Hemoglobin Standard are as follows:

Cell of American Pathologist Panel in Chicago  
 ICDSCS are working place in Detroit, Michigan  
 responsible for the production of certified reference standards

1 That cyanmethemoglobin be adopted as a standard in clinical hemoglobinometry

2 That the standard be characterized spectrophotometrically on the basis that the extinction coefficient of one milligram atom of iron ( $c = 1$  mg atom of iron per liter,  $d = 1$  cm) in the form of cyanmethemoglobin at a wavelength of  $540 \mu$  is 11.5

3 That 0.338 per cent (w/w) be accepted as the iron content of hemoglobin (molecular weight of 16,520 per gram atom of iron in accordance with the recent recommendation of the Protein Commission section of Biological Chemistry of the International Union of Pure and Applied Chemistry and that a factor of 1.652 be used in calculating hemoglobin in mg per 100 ml from millimoles per liter

4 That the standard be distributed as a single concentration of not less than 55 mg of cyanmethemoglobin per 100 ml

5 That solutions be distributed in brown glass containers and in sterile condition

6 For the present it is recommended that solutions should be used as standards for a period not to exceed nine months from the time of preparation. This dating period is based upon the results of the National Research Council field trial. As experience accumulates with commercially prepared samples an extension of the dating period may well be found to be justifiable

7 That the standard be prepared from either crystalline hemoglobin or washed erythrocytes

8 That commercial producers of the standards submit representative specimens from each lot to the College of American Pathologists Prudential Plaza Chicago 1, Ill for certification (a) that the concentration of cyanmethemoglobin is within  $\pm 2$  per cent of the value stated on the label (b) that the solution is substantially optically clear and (c) that it is microbiologically sterile

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Sw l d.

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### KNEE INJURIES IN MILITARY PERSONNEL

Knee injuries in actively serving military personnel are an important cause of loss of manpower both from a stand point of prolonged convalescence and permanent partial disability. The age group of the serving soldier is we think responsible for the frequency with which we find knee injuries in these men. They are a young healthy vigorous group who subject themselves to frequent and strenuous trauma in their daily training and are prone to engage in vigorous sports as well. In judging the final results of treatment in post operative cases one must not accept too readily the statistics on civilian personnel and attempt to apply them to military patients. A civilian patient who may be considered to have a completely satisfactory recovery allowing him to meet all the demands of a normal civil life may from a military viewpoint not be considered fit to undergo the strains of modern military training or battle. It is interesting to note that most of the acute knee injuries seen especially those involving tears of the menisci are sustained either in training or on the sports field and are not due to the motor vehicle accident which supplies so many of the traumatic cases seen in the surgical wards of our army hospitals in peacetime.

—G W CHAPMAN Maj R C A M C  
in *Canadian Services Medical Journal*  
p 486 Sept 1957



## Clinicopathologic Conference

U S Naval Hospital Chels Mas  
U S Naval Station Hospital Naples Italy

### JAUNDICE AND FEVER

#### Case 1

**Summary of Clinical History** A 30 year old Caucasian was admitted to the hospital because of general malaise and vomiting. Two days previously he had noted the onset of fever followed by increasing weakness and vomiting. Anorexia was prominent and he believed his skin was getting yellow.

**Physical Examination** The patient was an acutely ill man who appeared apprehensive and toxic. The skin and sclera were icteric. The heart and lungs were normal. The liver was palpable at the costal margin and was moderately tender. The spleen was just palpable. His temperature was 104.2 F and his pulse was 86 per min and the respiratory rate was 20. Blood pressure was 86/54 mm Hg.

**Laboratory Studies** The hemoglobin was 13.5 grams per 100 ml. The white blood cell count was 8,000 per  $\mu$ l with 49 per cent neutrophils, 40 per cent lymphocytes, 2 per cent monocytes, 2 per cent eosinophils, and 7 per cent basophils. The urine contained bilirubin. Dark field examination of serum and urine for spirochetes was negative.

**Course in Hospital** The patient continued to vomit and was given fluids intravenously. He ran a spiking temperature (104 F) and maintained a relatively low pulse (under 100). The vomitus

C p C I D R g g MC USA C mm d g Off F m th L b y S  
C pt Fr J M Mah MC USN Ch f  
C p M y Sh pp MC USN C mm d g Off

became brown in color and was positive for occult blood. In the next four days the patient developed severe hiccuping, intermittent in character but very uncomfortable. The liver remained palpable and tender. The white blood cell count rose to 15,000 per  $\mu$ l with 95 per cent neutrophils and 5 per cent lymphocytes.

On the fifth hospital day the patient's temperature dropped from 103° to 98 F. His pulse rose to 100. He stated that he felt much better and that he was hungry. He was allowed clear fluids and soft custard. He had no further vomiting. That evening, although confined to bed, he got up, and sat for awhile. Later he returned to bed and while there he sat up suddenly because he could not breathe and felt cold. He went into shock rapidly, developed dyspnea, and expired.

### *Case 2*

**Summary of Clinical History** A 34 year old plane captain was admitted to the hospital because of fever, malaise, and vomiting. Jaundice was noted on the day of admission.

His plane had one crew member admitted to the sick list (case 1) and a third recovering from infectious hepatitis at the U S Air Force Station Hospital, Dhahran, Saudi Arabia. All the crew members had been inoculated against yellow fever. The crew were exposed to rats. The plane, normally based at Dhahran, had departed with the same crew, for Aden, British Protectorate, one month prior to the patient's admission to the hospital. The plane crew remained in Aden four days before returning to Dhahran. Five days later the plane took off for Jidda, Saudi Arabia, and Asmara, Eritrea. In the next few days the plane flew between Cairo, Egypt, and Dhahran, Saudi Arabia. Sixteen days prior to the patient's admission to the hospital the plane and crew took off from Dhahran for Massaua, Eritrea, then going to London via Cairo, Beirut, and Naples.

**Physical Examination** The patient appeared acutely ill, jaundiced, and unusually toxic. The heart and lungs were normal. The whole abdomen was tender. The liver edge was just palpable below the costal margin on deep inspiration and was tender. The spleen was not palpable. The temperature was 100.8°F, the pulse, 96, and the respirations 20. The blood pressure was 108 systolic and 74 diastolic.

**Laboratory Studies** The hemoglobin was 10 grams per 100 ml. The white blood cell count was 6,500 per  $\mu$ l on admission, rising to 8,200 during hospitalization. Differential count revealed 61 per cent neutrophils and 39 per cent lymphocytes, repeat differential examination was unchanged. The urine contained 60 mg of albumin, and microscopic examination revealed 6 erythrocytes and 1 granular cast per high power field. Kahn test was negative. Dark field examination of serum for spiro

chetes was negative Cephalin cholesterol flocculation test was 3 plus in 48 hours thymol turbidity was 5 MacLagan units Total protein was 5.0 (albumin 2.4 globulin 2.6) grams per 100 ml. A thin blood smear for malarial parasites was negative. No pathogens were found on stool culture.

**Course in Hospital.** The patient's temperature ranged between 99° and 104° F with the pulse varying between 78 and 90. Hematemesis occurred on the second hospital day and continued. He had several episodes of epistaxis. Hiccup began on the fourth hospital day and continued thereafter until death. Small liquid tarry stools bothered the patient and were associated with cramps. On the evening of the fourth hospital day he complained of sudden loss of vision, became rapidly dyspneic, had a short convulsion, and died.

### DISCUSSION

**Distinction.** Feature of these two cases that impressed me was the similarity of signs and symptoms and the acute fulminating course of febrile disease associated with jaundice in two young men stationed in the tropics.

The past history of these two patients is not given but inasmuch as they had been on active duty as flight personnel we can assume that both of our patients had been healthy men. Both had been on duty together. They had the same type of immunization including yellow fever. Both served in the same area where tropical diseases are known to occur. A third crew member was recovering from infectious hepatitis.

The onset was sudden with malaise and vomiting, followed by a septic type of temperature associated with jaundice. The patients were acutely ill, toxic, and both had a palpable and tender liver. Mild splenomegaly was noted in one of them. The other had a tender abdomen. The vital signs given on the dates of admission are similar: low fever, relatively low pulse rate (under 100), slightly labored respiration, and low blood pressure. The only apparent clinical difference was that the second case entered the hospital sooner in the course of his illness than the first one.

From the laboratory standpoint the only difference is that we have given more studies in one case than in the other. The white blood cell count was normal in both patients; the differential showing slight lymphocytosis.

The hospital course in the first case was marked by spiking temperatures with the pulse rate remaining below 100° F, hematemesis on the third day of illness, white blood cell count rise to 15,000 with a shift to the left. On the seventh day of illness the patient's

temperature dropped suddenly to 98°F, the pulse rose to 100 and subjectively he felt much better. He got out of bed suddenly went into acute collapse, and died.

The hospital course in the second case was stormy with the patient's temperature ranging between 99° and 104 F and the pulse remaining below 100. Hemorrhagic manifestations became evident in the third day of his illness in the form of hematemesis, epistaxis and melena. The white blood cell count remained low, however, a left shift was noted. This patient died suddenly after loss of vision, a brief episode of dyspnea and a short convulsion. One brief remark on the hiccups, persistent hiccuping occurred in both instances after the onset of gastric hemorrhage and its cause could be explained on the basis of gastric irritation.

Since the symptomatology in both cases was alike I shall assume a common cause. This tends to preclude diseases other than those due to poison or infection. From the standpoint of a possible toxic cause, a wide variety of chemical compounds including dinitrobenzene, trinitrotoluene (TNT), picric acid, dinitrophenol, phosphoreted hydrogen, some of the anesthetics, phosphorus and heavy metals are well known causes of acute yellow atrophy. A similar picture may arise after ingestion of the male fern and poisonous mushrooms.<sup>1</sup> During the past few years attention has been paid to a disease mostly seen in Jamaica but also in India and Egypt, morphologically characterized by occlusion of the hepatic veins. This entity is referred to as "veno-occlusive disease of the liver." It is observed mainly in children but also among adults. All cases described occurred in poorer economic groups where malnutrition or subnutrition may be present, yet it is believed that some toxic agent plays a major role in this disease. In all the published cases the patients habitually drank a variety of bush tea. These are infusions of various herbs, seeds and roots. Senecio (ragwort) poisoning may exhibit the same features as veno-occlusive disease. The course of this disease is either acute, subacute or chronic. The acute form of veno-occlusive disease is characterized by the sudden development of abdominal pain, hepatomegaly and ascites. Vomiting is common. Some of the patients rapidly develop liver failure and die.<sup>2,3</sup> It is quite unlikely that our pilots were malnourished or had partaken of "bush tea," yet some reported cases closely resemble the clinical picture that they presented.

This leads to the discussion of the infectious origin of the cases under consideration. One crew member was said to be recovering from infectious hepatitis, that could well be a clue. The incubation period of infectious hepatitis is normally given as between two and six weeks, and these patients could have been exposed to infectious hepatitis through contact with the third crew member. Lucke and Mallory in 1946 gave a thorough description of the fulminant form of epidemic hepatitis among members of the armed services stationed



all over the world. The incidence of occurrence of this form was high in the Mediterranean area as elsewhere. Of the 196 fatal cases of epidemic hepatitis 94 (53 per cent) died in less than ten days, most frequently between the fourth and ninth day. The clinical picture was characterized by a short and stormy course, either in the form of the infectious type with high temperatures, malaise and general chills, or a gastrointestinal type with anorexia, nausea and epigastric discomfort predominating. Jaundice usually appeared by the second or third day. In nearly all cases the pulse rate was elevated when there was fever. The features tending to differentiate the diagnosis in the patients under discussion from acute fulminating hepatitis is, in my opinion, the different course of the disease in these cases. There are no relapsing temperature and in fulminating hepatitis there is no well day, as we were informed that the first case had. The mode of dying is quite different; patients with fulminating hepatitis usually going into a deep coma preceded by cerebral symptoms of a more gradual onset.

Inasmuch as both patients were stationed in tropical regions, e.g. in Saudi Arabia, the East Coast of Africa, etc., any number of infectious diseases occurring endemically or at times in epidemics must be considered. Let us confine our attention to those diseases that are associated with fever and jaundice. Dengue, Rift Valley fever, echinococcosis and visceral leishmaniasis (kala-azar) are readily ruled out by their entirely different clinical course, which is mostly milder, more chronic in the case of dengue and dengue-like fevers, or usually associated with a skin rash in cases of leishmaniasis.

Acute amebic hepatitis developed during the incubation of the intestinal infection or during remission. Generally there is a history of amebic infection. There is right upper quadrant pain with an enlarged and tender liver. The fever is high and the white blood cell count usually ranges between 20,000 and 30,000 with a marked increase of the neutrophils. I think that the lack of information in the history is regarded to intestinal parasites and the initially low white blood cell count are sufficient reasons to exclude the possibility of amoebic hepatitis.

The relative bradycardia, the initial absence of leukocytosis and the severity of the clinical picture made me think of typhoid fever. Formerly, it was believed that typhoid fever seldom occurs in the tropics. It has been commonly confused with malaria and in the southern part of the United States it was common to diagnose typhomalarial fever. The complications in typhoid fever include intestinal hemorrhage, intestinal perforation, pneumonia, meningitis, myocarditis and sometimes terminal jaundice. However, a well day is not seen preterminally in cases of severe typhoid fever. In addition, these patients being members of the armed services, certainly were immunized against typhoid, making this diagnosis more unlikely.

The protocol mentions that the crew were exposed to rats but adds that the urine and serum were negative for spirochetes by dark-field examination. Of the leptospiroses we have to consider Weil's disease and relapsing fever.<sup>6</sup> If we compare the picture of Weil's with the cases in point we find a few striking differences. Several of the cardinal features of Weil's disease are missing, namely the myalgias, the conjunctivitis, and the headache. Also in Weil's disease the onset of jaundice is on the fifth or sixth day of illness. The search for spirochetes by means of dark field examination is not always successful but they may be found in the blood within the first five days of illness. A search of the urine would be futile because positive results are not expected until the second week of illness. We find fewer differences when we consider relapsing fever. In the African tick fever a high white blood cell count is noted and the pulse rate is accelerated. I think we may dismiss these diseases.

Allow me to quote here the description of another disease taken in part from Cecil's Textbook of Medicine: "Yellow fever is an acute viral disease characterized by sudden onset, prostration, moderately high fever, a pulse rate slow in relation to temperature and when severe, by vomiting of altered blood, albuminuria and jaundice. It is endemic in the tropical rain forests of Africa and South America. Fatal cases often exhibit hiccup, copious vomiting of altered blood, tarry stools and anuria. Death occurs most frequently from the sixth to the ninth day."<sup>7</sup> Leukopenia is sometimes pronounced.

At first I thought that the protocol presented nothing more than a textbook description of yellow fever. However, there is one stumbling block. Both patients were inoculated against yellow fever. Vaccination against yellow fever is said to be very effective and antibody titers are known to persist for at least 6 years. One of the most conclusive evidences that vaccination is an effective procedure in protection against yellow fever is the fact that since introduction of yellow fever vaccine no accidental cases of the disease have occurred. Therefore the fact that the patients had been inoculated against yellow fever is strong evidence against that disease.

Up to this point most of the diseases discussed were chosen under the assumption that the major pathologic condition was massive liver necrosis or at least extensive hepatocellular damage. Let us therefore examine the protocol critically and see whether we find indications justifying such an assumption. In the first case we are informed that the patient was jaundiced; however, no mention is made that the jaundice deepened, e. g. that "liver cell destruction" was progressive. The same is true in the second case. The liver was palpable and tender in both cases but no mention is made as to whether this liver enlargement was progressive or regressive. Liver enlargement is seen in many other conditions, quite often on the basis of congestion, and in acute congestion this enlargement is accompanied by pains in the liver area and tenderness of the liver to palpation.

The urine was positive for bile in the first case. This merely means that the patient's serum bilirubin was elevated. We know, however, that the direct bilirubin of serum has a much lower renal threshold than the indirect variety; therefore bilirubinuria is rare in the form of hemolytic icterus. In occasional cases, however, bilirubinuria is found if liver damage has taken place as a secondary result of anemia or hemolysis. That liver damage may have occurred is suggested in the second case by the abnormal cephalin flocculation and thymol turbidity findings. These tests are by no means diagnostic of severe hepatic destruction. I think that one is justified in considering the possibility that the jaundice may be on the basis of blood destruction rather than primary liver disease. Insofar as the hemoglobin is concerned we only have two bits of information: 13.5 grams of hemoglobin early in the disease of the first patient and 10 grams later in the course of illness in the second case. If one assumes that the patients were healthy prior to their illness and were ill for only two days before the examination one wonders somewhat about the value of 13.5 grams of hemoglobin in a young male. The evidence is definite of reduction of the hemoglobin content in the second case, but whether on the basis of blood loss or on the increased hemolysis cannot be determined.

However, I think the question of blood destruction justifies the inclusion of malaria in the differential diagnosis. The incidence of malaria is quite high in the tropics. The incubation period in vivax and falciparum infection are roughly the same, between 9 and 14 days. As far as the clinical picture is concerned there is such a great variety of different forms reported that a lengthy discussion of the problem may still not give a clear picture. Therefore I will discuss the possibility of malaria only on the basis of the information given in the protocol instead of trying to list all the possible clinical forms of malaria infection. The most probable is *Plasmodium falciparum*, the etiologic factor in malignant tertian malaria. The course of the disease may be short and violent, starting with a fever which persists in a spiking manner. Our first patient had a good day on the seventh day of his illness. I do not think that in any other disease which we have so far discussed, including fulminating hepatitis and yellow fever, the patient feels well and gets out of his bed on the same day he develops illness, and vomiting is a feature of many infectious diseases and is also prominent in malaria. Bradycardia occurs both in dengue and yellow fever, but here more as an absolute phenomenon where our patients showed a relative bradycardia, the pulse rate remaining under 100.

The white blood cell count in our cases was normal on admission. The development of leukopenia is usually observed in yellow fever, dengue, and sandfly fever at the onset of the disease, while the count in malaria is usually about or below normal level. The neutrophils do not usually show relative increase as generally seen in bacterial

infections In the former diseases mentioned one almost invariably finds a lymphocytosis

In malaria, jaundice may occur on the second day, earlier than in yellow fever In malaria the liver is usually palpable the spleen however, may or may not be felt in the acute stage Splenomegaly is more a feature of the chronic forms of malaria Furthermore, it depends on the type of plasmodial infection being more pronounced in infections with *Plasmodium vivax* but less with *Plasmodium falciparum* Hepatic involvement is almost invariably present in malaria which explains the discrepancy between visible jaundice and minimal evidence of hepatic disease in other words the jaundice is more on the basis of hemolysis than liver damage

Both patients had signs of renal involvement Albuminuria is commonly seen in high fever but when accompanied by red blood cells and casts the renal lesion is thought more serious Malarial nephritis occurs in falciparum infection but is less common in other malarial infection Renal involvement is also noted in yellow fever and is most pronounced in Weil's disease

No mention has been made of two symptoms hiccups and hemorrhagic manifestations Both of these symptoms are pronounced in the course of yellow fever and bleeding can occur in fulminating hepatitis the mechanism probably being a disturbance in prothrombin production Hemorrhagic tendencies also occur in malignant malaria the mechanism here thought of being due to congestion of the capillaries Hiccups epistaxis and blood in vomitus and stool are also features of malignant malaria

Human malaria is an infection of the erythrocytes When the trophozoite matures the red blood cell is destroyed Large numbers of infected erythrocytes are destroyed and phagocytized before maturation of the parasite This results in a rapid loss of erythrocytes Furthermore Wong<sup>12</sup> in 1945 proposed that there must be an unidentified factor present during a paroxysm which inhibits full oxygenation of the blood hemoglobin Destruction of large numbers of red blood cells releases parasites pigment and erythrocytic debris This throws a tremendous burden on the phagocytic cells of the body mainly cells of the reticuloendothelial system which show generalized swelling The blood flow through the capillaries is slowed sometimes to the point of stasis The question of whether or not there is true plugging of the capillaries is not yet solved For unexplained reasons these changes have a predilection for the capillaries of the brain They also are more frequently found in organs or systems to which the most prominent clinical features were referable I think it conceivable to explain the hemorrhagic features of our patients on the basis of congestion in the gastrointestinal tract On the same basis one also can explain the hiccups

It is difficult to explain the mode of death in both cases unless one assumes that on the basis of the pathophysiology of malaria

anoxia and acute capillary congestion of the vessels of the brain and the heart were the final events

On the basis of clinical manifestations three types of malignant malaria have been described (1) cerebral manifestation (hyperpyrexia coma) (2) algid manifestation (diarrhea fever) and (3) bilious remittent fever. It also is emphasized that mixed form can occur.

My clinical diagnosis is pernicious or malignant malaria due to *Plasmodium falciparum* most likely of the bilious remittent fever type. I admit however that it is difficult to explain why these two airmen simultaneously developed such a fulminating form of malarial infection and in any type of infectious disease the final diagnosis comes in most instances from the laboratory.

Doctor Si: There is very little left to say. I will however differ about everyone being vaccinated as they should in the armed services. Certainly there were a number of individuals who missed vaccination for smallpox during World War II and the Korean Conflict. The clinical phase of both these cases is so clearly associated with yellow fever that I would not be surprised if this were the diagnosis. We know that this was an endemic area. Onset was rapid with high fever, low blood pressure, vomiting of coffee-ground material, hiccups, sudden and what seemed unexplained death. When patients appear ill from yellow fever in the first stage which was the case in both these individuals, a fall of temperatures in the middle of the course is usually not uncommon and may be an unsettling event. A return of fever with shock and sudden death is consistent with yellow fever.

Being in cardiology I was interested in the sudden death and low blood pressure which were consistent with myocardial infarction. As far as fulminating hepatitis is concerned and as Doctor Artzschmer has pointed out, early deaths are very similar to acute yellow atrophy and the patients die in a state of coma. Serum hepatitis is not associated with fulminating fever and would be less likely. An embolus as the immediate cause of death does not appear to be consistent. As far as *falciparum* malaria is concerned that I have seen acute yellow fever. I have not.

*Falciparum* malaria is an acute disease but as far as we know the sudden and quick deaths are in those who have cerebral malaria. Doctor Kretzschmar brought out the possibility of Weil's disease with the characteristic signs of renal involvement, chills and fever. The chills appear after a return of fever and manifestations of bloody diarrhea or uremia.

With this type of picture I believe that these individuals missed or avoided yellow fever vaccination. I do not think they had *falciparum* malaria but rather yellow fever.

Doctor MacGregor I thought of using the reverse approach to these cases and first made up a differential diagnosis then went through the list to see which were the most typical Granting that there were four entities which should be considered namely Weil's disease infectious hepatitis fulminating malaria, and yellow fever I chose yellow fever largely on the basis of epidemiology and because it seemed to fit the clinical factors that are known to us

Yellow fever explains the course of two similar cases and a possible third that occurred at about the same time in personnel who had been similarly exposed These points seem to me to be against the other three entities I think that the probability of two people being exposed to rats and being infected is less likely In the same way having two cases of fulminating hepatitis at the same time is most unlikely I think that many aspects of these cases including the diarrhea hematuria convulsions and death were consistent with yellow fever and that such a diagnosis is indicated

Doctor Delabarre J I have never seen a case of yellow fever or Weil's disease but think it would be most unlikely that both patients would come down with the same type of malaria with the same termination I think yellow fever is the most likely diagnosis Vaccination for yellow fever is not 100 per cent effective and we do not know when they were vaccinated

Dr Kretzschmar's diagnosis

Cases 1 and 2 Pernicious or malignant malaria, due to *Plasmodium falciparum*, most likely of the bilious remittent fever type

Diagnosis of Drs Sise MacGregor and Delabarre

Cases 1 and 2 Yellow fever

### PATHOLOGIC FINDINGS

Doctor M Mahon The spleen in case 1 weighed 700 grams and in case 2 750 grams The livers weighed 2 125 and 2 500 grams respectively the kidneys 575 and 650 grams and the hearts 500 and 550 grams The spleens were tense with a thin capsule that tore easily The pulp was soft friable and devoid of recognizable architecture The livers were yellow green to gray congested and firm The architecture showed an interlacing group of swollen gray cords with irregular dark green pin point dots throwing the gray cords into relief Both hearts were enlarged and markedly dilated the auricular walls were parchmentlike in thinness The myocardium was soft friable and granular The lungs were heavy and wet The kidneys on section showed a swollen bulging cortex that was sharply demarcated from the congested medulla

Capt J h B M cGr g r MC USN Chi f M d 1 S rv ce

C mdr Ev r tt M D I barr Jr MC USNR U S V t r n Adm: strat on H sp tal  
W t H C

Microscopically the spleen showed marked congestion with washing out of the cells in the pulp. There were many macrophages filled with pigment. Some of the follicles were hyperplastic but others tended to be replaced by larger variable sized cells with hyperchromatic nuclei (fig. 1). The liver showed empty sinusoids lined by numerous large Kupffer cells filled with pigment (figs. 2 and 3). The capillaries of the heart and intestines were filled with paritized erythrocytes and pigment debris (figs. 4 and 5). The kidneys showed degeneration of the tubular epithelium.

#### Pathologic diagnosis

#### Acute fulminating malaria

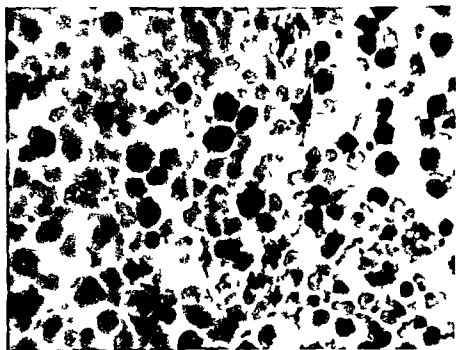
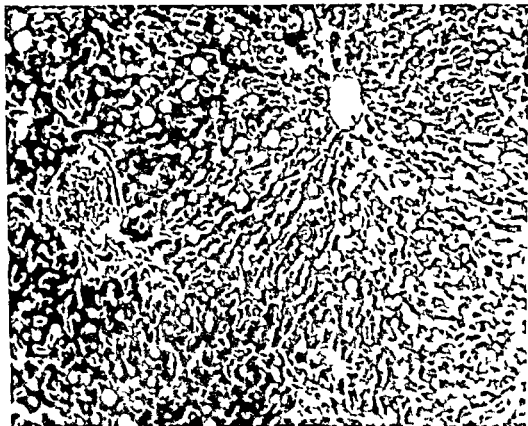


Fig. 1 Spleen. Large atypical macrophages filled with pigment and debris. (x430)

Even though we were in a so-called malarious belt and had dealt with transient fever all over the Mediterranean area, the Near East and Africa, we had not seen a case of malaria in the previous five years. Because of this we have not been malaria conscious. The clinical course of the disease in these two men certainly did not show the typical distinct febrile paroxysms with the cold, hot, and sweating stages. There are many sorts of circumstance that could have the way for the pernicious form among which are alcoholic, excessive fatigue, high external temperature, and a continuation of customary activity. It was postulated that these men who flew their plane on a rather

heavy schedule probably were fatigued yet continued their activities even when indisposed

Pernicious manifestations fall into three general groups namely the cerebral algid and gastrointestinal plus a miscellaneous grouping. It was not easy to separate these cases into the various subdivisions of pernicious malaria and to say that they were purely algid, cerebral gastrointestinal or that they developed black water fever. Some symptoms would suggest the gastrointestinal phase. Black vomitus occurred in both cases and tarry diarrhea occurred in case 2. In this case many pigment granules and parasites were seen in the mucosal capil-



*Figure 2. Liver. Low power view showing empty sinusoids containing large Kupfer cells ( $\times 120$ )*

laries of the gastrointestinal tract (fig 5). The clinical history of delirium, agitation, loss of vision and convulsions noted in case 2 was very suggestive of cerebral malaria. The pathologic findings of greatly enlarged spleen, kidneys and liver larger than those usually seen in acute falciparum malaria, together with the microscopic findings of early hemoglobinuric nephrosis suggested the diagnosis of black water fever, but the complete clinical and microscopic picture of black water fever does not seem to be proved by the clinical course and the autopsy findings. The myocarditis and pulmonary edema in case 1 with the terminal episode of shock and dyspnea suggested that death was a result of cardiorespiratory failure.





Fig 3 L S d b u g k p f f c l l f l l g d a n d i f f d  
u t h p g m i a n d p a t (x430)



Fig 4 H i C p l l a y f l l d u t h p i z d e r y t h r o c y t (x430)

The epidemiology of their disease if it was *Plasmodium falciparum* malaria is interesting. These men were operating in areas where malaria is highly endemic and in the past epidemic Central Arabia is notorious for oasis fever. In times past malaria has been epidemic in Aden. In conversations with the British Commandant it was learned that several cases of malaria have been reported there in the past few years. The men stated that they were bitten by mosquitoes while staying in Asmara. It was unlikely that malaria was contracted in Asmara unless they brought the malaria bearing mosquitoes with them.

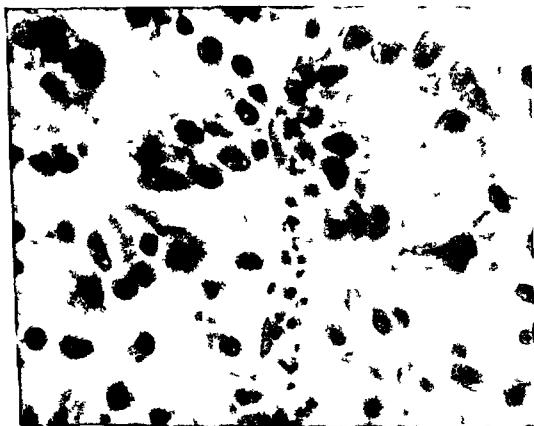


Fig 5 Small intestine (jejunum) Capillary showing pigment debris and pale erythrocytes. (x 430)

Asmara is located 7 000 feet above sea level and Italian surgeons who operated in this area during the last war said they were of the firm conviction that no malaria was present in the high plateau in Eritrea. That leaves Massaua in Eritrea, which is at sea level and is known to be malarious. If this was the first acute attack and from the clinical symptoms and the pathologic findings it seems to have been then the mean incubation period of about 13 days would fit well with their stay in Massaua Eritrea.

In conclusion it is well to bear in mind that although great strides have been made in the control of malaria it is still a common disease in many parts of the world. In days of fast travel when many military personnel and tourists pass through or visit endemic areas this dis

ease continues as a problem. In a recent communication from the Armed Forces Institute of Pathology concerning these cases, one of the staff made the following comment which may be of particular interest to clinicians: "To my knowledge these two cases will make a total of four cases of fulminant malaria recorded here within the past four years in which malaria was not diagnosed antemortem. In one more case the diagnosis was made when the patient was moribund." James quoted in *Malaria* as follows: "It is characteristic of many pernicious symptoms that they tend to prevent the prompt diagnosis of the disease. They may do so either by presenting in a prominent manner a symptom which strongly suggests some other condition than malaria, or by presenting in a patient who is obviously very ill, an almost complete absence of what are known to be the usual clinical signs of malaria."

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## EPIDEMIOLOGIC STUDY OF TUBERCULOSIS IN THE U S NAVY AND MARINE CORPS

( Methodology and Individual Factors

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**T**HE problem of controlling tuberculosis in the Armed Forces is still of considerable importance to the nation, despite the fact that in the U S Navy, as an example, the incidence of the disease has dropped from 6.8 per thousand per annum in 1903 to 0.8 in 1954.<sup>1,2</sup> It has been variously estimated that each case of tuberculosis in the Armed Forces costs the government about \$60,000 when cost of training, hospitalization, and disability benefits are considered.<sup>3</sup> In the Navy in 1953 there were 742 persons diagnosed for the first time as suffering from tuberculosis who were adjudged as having contracted the disease while in service.<sup>4</sup> The government assumed responsibility for the care and disability benefits accorded these persons. The ultimate cost, then, of tuberculosis in the Navy for the year 1953 might be estimated as amounting to some \$44,520,000.

In view of the continuing importance of tuberculosis in the Armed Forces and the nation it is evident that a more complete knowledge of the epidemiology of the disease as it occurs in one or more branches of the Armed Forces should be of assistance to those charged with the protection of the health of service members.

### Purpose

The primary purpose of this study was to attempt to determine what factors, such as personal attributes, environment, and particularly characteristics of service life, have been associated with excessive risk of development of tuberculosis in the U S Navy and Marine Corps. A secondary purpose was to aid in the evaluation of procedures designed to screen out tuberculous

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recruits prior to entry into the service and to find those cases of tuberculosis which might develop in service personnel after enlistment. Other branches of the Armed Forces may find the data in this study helpful in deciding whether they should adopt certain tuberculosis control procedures now practiced only by the Navy. These procedures are specifically the routine tuberculin testing of all recruits and the provision of annual x ray examinations of the chest for all enlisted as well as officer personnel.

### Previous Studies

For many decades there has been interest in the influence of environment and host factors in the epidemiology of tuberculosis in military industrial and institutional populations as well as in civilian populations. A limited review of the literature of the past 20 years on the subject reveals at least 74 articles dealing with the epidemiology of tuberculosis in various military forces in Europe and the Americas. An observation common to most of these studies is that military service particularly during times of war exerts an unfavorable influence on the incidence of tuberculosis in young adult males.

The Medical Department of the U S Navy has carried out studies on tuberculosis over the past 20 years or more. The work of Britton Charter and co workers is particularly noteworthy. Most studies however have dealt with mass data extracted from routine summaries noted on punch cards or taken from group statistical records. These studies have been descriptive of the distribution of tuberculosis within the services by such factors as age sex race rank length of service severity of disease and occasionally by occupation. Satisfactory epidemiologic analysis of these data has been troublesome since the numbers at risk in each category frequently have not been determined. Again in past studies the term tuberculosis has often been rather inclusive. Cases of pulmonary infiltration of unknown etiology have been included.

Two recent studies are particularly pertinent to this topic. The first by Long and Jablon is a study of tuberculosis in the U S Army in World War II. The main purposes were to determine the efficacy of x ray screening methods employed at induction and to delineate epidemiologic factors related to the occurrence of the disease in service. This study utilized the case control approach. The other by Palmer and associates<sup>11</sup> investigated the subsequent incidence of tuberculosis in naval personnel who had been through a naval training center where their tuberculin status was determined. It was concerned especially with this factor and with the influence of body build on susceptibility. The approaches and findings of these two studies were known to the authors and were most helpful in our

investigation, they will be further discussed at a later point. Incidentally, a few of the tuberculosis cases analyzed in this report are presumed to have entered in Palmer's analysis as well.

## METHOD OF STUDY

### Choice of Study Group and Method of Analysis

Since 1949, the Navy has routinely tuberculin tested all new recruits, thus, this service affords an unusual opportunity to study a large population, uninfected on entry into the service. Other advantages, shared by the other armed services, are the availability of uniform personnel records providing information on service conditions and types of duty, and of detailed medical records with considerable uniformity of diagnostic standards, nomenclature, and procedures. It was therefore decided to analyze the Navy material.

Three general methods of epidemiologic study were theoretically possible. The first was to relate the cases of tuberculosis to the service population out of which they arose. This was impossible because for many of the factors which it was desired to study, the number of naval personnel at risk was not known and could not be determined from service personnel records. The second was to follow up individuals after ascertaining their status with respect to each characteristic and in this way to determine differential incidence rates. This method was possible and would have given the most reliable information, but would necessitate an expenditure of time, effort, and funds beyond the available resources. The third approach, which was necessarily adopted, was the comparison of a series of cases with a suitable series of controls.

A number of workers have pointed out the uncertainties of selection involved in study of groups of people hospitalized for a disease, and some have even denied the validity of such an approach. It should be pointed out that these objections have much less force where one is dealing with a hospital system, and can be confident that nearly all recognized illnesses occurring in members of the community (in this case a military service) will be hospitalized within the service and recorded as cases in the service wide record system.

### The Study Group

Cases of tuberculosis diagnosed in 1953 and 1954 were chosen for study because case records of this recent period were generally complete and available and because foreign service and combat experience during the Korean Conflict could be considered. Both cases who were tuberculin positive and tuberculin negative on entry were included though many of the analyses pertain only to the originally tuberculin negative group. *P. acti*

cally all included cases entered the service in 1949 the year when service wide tuberculin testing of Navy recruits was adopted or subsequently

Some cases of tuberculosis developing in 1953 1954 were probably omitted from the study for such reasons as failure to detect lesions on roentgenograms omission of roentgenograms or erroneous diagnoses

The diagnosis pulmonary infiltration of unknown etiology (Code 0070 of the Joint Armed Forces Statistical Classification and Basic Diagnostic Nomenclature (BDN 1949) is frequently employed by the Navy for cases where the clinical and roentgenologic findings are not considered sufficiently characteristic to warrant a specific diagnosis of tuberculosis In official reports these cases are sometimes classified under tuberculosis No person with this diagnosis was included in the study because it was believed that only well supported cases should be included On the other hand proof of diagnosis by recovery of *Mycobacterium tuberculosis* was not required because of the very thorough and careful diagnostic study of all cases in the service and the belief that the number of tuberculosis cases that would be erroneously excluded by such a requirement would exceed the number of erroneously included cases if demonstration of the organism was not a criterion of acceptance Table 1 shows that *Mycobacterium tuberculosis* was recovered from 296 (73 per cent) of 405 persons in the study group and that there was not a significant

TABLE 1 Demonstration of *Mycobacterium tuberculosis* at final diagnosis in patients initially classified as pulmonary infiltration of unknown etiology —all persons

D i a g n o s i s I n i t i a l t u b e r c u l o s i s	S t u d y g r o u p									
	N e g a t i v e		D i a g n o s t i c		P o s i t i v e		U n k n o w n		T o t a l	
	N	P	N	P	N	P	N	P	N	P
Y o u n g	171	73.0	6	75.0	66	80.5	53	73.0	296	74.6
N o n	63	27.0	2	25.0	16	19.5	20	27.0	101	25.4
S u b j e c t	234	100.0	8	100.0	82	100.0	73	100.0	397	100.0
R e m o v e d										
	2		0		4		2		8	
T o t a l	236		8		86		75		405	

R e d h w d f a r h f g m w t h g l t.  
I f m b l g m g

difference in this regard between those who were tuberculin positive, tuberculin negative, or untested on entry into the service

Thus, it is to be expected that a very small number of persons erroneously diagnosed as having tuberculosis were included, and a somewhat larger number who did have tuberculosis were excluded from the study. The probable effect of the first error is to reduce a little the size of any true differences between the study group and the controls, the latter error should have no effect unless the erroneously excluded cases have characteristics different from those of the positively diagnosed cases

In resumé, the group termed the study group of tuberculosis cases consists of all those individuals who were first diagnosed as having tuberculosis while in the Navy or Marine Corps in 1953 or 1954, and whose first entry into service occurred in 1949 or later. All cases with a final diagnosis of any form of tuberculosis are considered. Those individuals known to have been tuberculin negative on entry into the service will be referred to as the basic study group. Many of the analyses will be limited to enlisted men of the Navy and Marine Corps, because they comprise nearly all the cases.

In many of the tables, data pertaining to all individuals, regardless of tuberculin sensitivity at induction, and data pertaining only to those who were tuberculin negative at induction, are both presented. Where this is done, the line designated "A" refers to the whole group and line "B" below, to the "basic study group" of nonreactors.

It will be noted in table 2 that case records were not received on 70 of the recorded cases of tuberculosis. To determine if there were any major characteristics of this absent group which might bias, by their absence, the attributes of the group actually received and studied, especially in relation to the control, the official Navy summary case cards of the 70 were tabulated. The "not received" group differed significantly in several respects from the study group. It must be borne in mind, however, that at least 10 or 11 of the 70 cases would have been rejected for study had they all been received, assuming that the 15 per cent over all rejection rate found to apply to the records received were to apply to them also. The principal reason for rejection of received records was service prior to 1949, hence a rejection of much more than 15 per cent of the group whose records were not received could be expected if this group included a high proportion of older men with longer service, as was found to be the case.

The proportion of enlisted male Navy medical and dental technicians was high in the "nonreceived" group; the inclusion of



all these cases would however only raise the percentage of this occupational category in the study group from 5.1 per cent to 6.6 per cent. The nonreceived group also included a higher proportion of minimal cases (31 per cent as compared with 21 per cent) and a corresponding deficiency in far advanced cases. However if all of these nonreceived case records were received and accepted the percentage of far advanced cases in the total study group would fall only 1.4 per cent. Nevertheless these differences must be kept in mind in subsequent discussion of these variables.

TABLE 2  
Navy Medical Corps 1953-1954

Category	Year 1953	Year 1954	Total
Case file U.S. Navy personnel	911	754	1665
Clinical diagnosis	696	564	1260
Duplicate	(85)	(35)	(120)
Tabular	(84)	(79)	(163)
Physical diagnosis pulmonary	(252)	(227)	(479)
Perforated with rupture 1949	(261)	(167)	(428)
Cases	(14)	(56)	(70)
Remained	215	190	405

Naval Medical Corps 1948-1954  
 Personnel file 478  
 Physical diagnosis 1949  
 Cases 1948-1954

### The Control Group

It was considered that the only control group which would yield the desired information and at the same time could practically be employed would be a series of cases of some other disease. Such a control group offers several advantages: it can readily be chosen on the same basis with respect to time factors as the study group and the medical records for major illnesses provide the information needed for the purposes of the study. The one serious disadvantage lies in the fact that every illness or accident involves some selection such that the group can not be regarded as entirely representative of naval personnel in general. In other words instead of the desired comparison the epidemiology of tuberculosis would be contrasted with that of another condition. A number of conditions and diseases such as accidents, upper respiratory disease, venereal disease, mental

disorders, allergic conditions, and dental conditions were considered and rejected because they were known or presumed to be selective in one way or another. Acute appendicitis was the condition which seemed to come closest to satisfying the requirements for a control illness. In order to study its distribution, a random sample of 20 per cent of all cases of appendicitis in the Navy and Marine Corps in the years 1953 and 1954 was compared with the composition of the services for the same years for those characteristics the distribution of which, in the service, could be obtained. This study showed that the appendicitis cases had a small but significant deficit of officers and of Negro personnel, and were younger on the whole than service personnel in general. This age difference is revealed by estimating attack rates per 1 000 population per year from the sample. The rates go down with increasing age in each year from 7 per 1 000 per year for personnel under 20 to 1.5 for personnel over 35. This would account for the deficiency of officers in the appendicitis sample.

There are also differences in length of service. These, however, are at least partly fictitious because inactive duty periods were counted in total service in the Bureau of Personnel records utilized for getting the composition of the entire Navy and Marine Corps, but not in the medical records from which the appendicitis data were taken.

While the agreement was not as good as might be hoped, further comparisons which were made between the appendicitis control series finally chosen and the Navy and Marine Corps as a whole, which will be presented later, provide a more encouraging picture. These comparisons are with respect to reserve status, rank, service occupation, tuberculin sensitivity, and height and weight. We need not be seriously disturbed by the differences in age, because the selection for time of enlistment and of diagnosis imposed in the study nearly eliminated age differences, nor by the differences in length of service because the control series was matched for length of service with the tuberculosis cases.

The control group chosen consists of individuals first diagnosed as having acute appendicitis (BDN 5500 5505) in the Navy or Marine Corps in 1953 or 1954, whose first entry into service occurred in 1949 or later. It was estimated that a 20 per cent random sample of all appendicitis cases would yield a sufficient number of records from which to derive a control sample. This was secured by drawing the records of all appendicitis cases with serial numbers ending in either 6" or 7". Because a number of variables to be studied, such as place and length of foreign duty, ship service and Korean experience depended on a close similarity between study and control groups with respect to length of service prior to illness, it was decided to

assigned to sea duty or foreign service there were seven females among the cases and only one among the controls

TABLE 4 *Comparison of duty assignments by sex and race*

Category	Case		Control	
	Male	Female	Male	Female
Navy				
Officer A	5	1	0	0
Officer B	2	0	0	0
Enlisted A	314	4	366	1
Enlisted B	185	0	253	1
Marine				
Officer A	3	0	0	0
Officer B	1	0	0	0
Enlisted A	76	2	116	0
Enlisted B	46	2	78	0
Total A	398	7	482	1
Total B	234	2	331	1

A = foreign duty assignment; B = domestic assignment

TABLE 5 *Military duty assignments by race*

Race	Case		Control	
	Number	Percent	Number	Percent
Caucasian				
A	351	90.2	469	97.5
B	211	91.3	324	97.9
Negro				
A	25	6.4	8	1.7
B	14	6.1	4	1.2
Ally				
A	13	3.4	4	0.8
B	6	2.5	3	0.9
Subtotal				
A	389	100.0	481	100.0
B	231	100.0	331	100.0
Unknown				
A	1		1	
B	0		0	
Total				
A	390		482	
B	231		331	

A = foreign duty assignment; B = domestic assignment

Of the controls, 17 per cent were Negroes, of the tuberculin negative controls, 12 per cent (table 5). However, 39 per cent of the entire personnel of the Navy and Marine Corps in 1953 were Negroes,<sup>4</sup> and probably nearly all persons of this race were enlisted men, data were not available for 1954. This discrepancy makes for uncertainty as to whether the control cases of appendicitis reflect the composition of the service with respect to race. In any case, even if one accepts 39 per cent as the true figure, it is still significantly lower than the percentage among the cases (64 per cent) and, of course, the observed percentages are markedly different. There was also an excess of "other races" among the cases, but the numbers for any single racial group are too small to be meaningful.

Religious affiliations were examined because of the possibility that they might reflect ethnic differences in susceptibility. It has been suggested that Jews have lower susceptibility to tuberculosis. No significant differences were observed between cases and controls in the percentages who were of each faith, but only six persons of Jewish faith were in the study.

#### Age at Entry Into Service and at Final Diagnosis

The age distribution of both groups was examined. As was expected the distribution of ages at entry in the basic study group and in controls was almost identical because the control group was matched by length of service to the study group and all men had less than 6 years of service. Relatively few enlisted men enter the Navy after age 21. The ages at final diagnosis differed slightly.

Information in the medical records on the level of civilian education prior to service was insufficient to permit this to be studied.

#### Tuberculin Sensitivity

The tuberculin reaction at entry into service was of particular importance. There were 75 cases and 115 controls for whom this was unknown.

Tuberculin testing of recruits in the Navy and Marine Corps has been done since 1949 at all basic training centers of these services. The standard test dose employed throughout has been 0.0001 mg of PPD. Injections are given and reactions are read after 72 hours (in no case earlier than 48 hours) by skilled medical technicians under the supervision of medical officers. Since the beginning of the program in 1949 the degree of reaction has been recorded in conformance with the standards of the National Tuberculosis Association as follows:

Negative - No induration

Doubtful - Trace of induration of 5 mm diameter or less

1 plus - Induration of more than 5 mm not exceeding 10 mm

2 plus - Induration of 10-20 mm diameter

3 plus - Induration over 20 mm in diameter and marked erythema

4 plus - Severe induration and an area of necrosis

While visiting the U S Naval Training Center San Diego Calif in February 1956 the testing and recording of recruits was observed, and the processing was found to be technically and administratively excellent. In addition it was noted that all recruits showing doubtful or positive reaction or having a history of contact with a tuberculous person were given a 14 by 17 inch x ray film examination in addition to the routine 70 mm film taken on all recruits at the station.

The composition of our case and control series with respect to tuberculin sensitivity is presented in table 6 and in figure 1.

TABLE 6. Tuberculin sensitivity of recruits

R	C		C	
	Nb	P	Nb	P
Type				
Negative	236	71.5	332	0.2
Doubtful	8	2.4	3	0.8
1 plus	86	26.1	33	9.0
2 plus	330	100.0	368	100.0
3 plus	75		115	
Total	405		483	
Doubtful percentage				
Doubtful	8	8.5	3	8.3
1 plus	29	30.8	16	44.4
2 plus	27	28.7	10	27.8
3 plus	24	25.5	4	11.1
4 plus	6	6.4	3	8.3
Total	94	100.0	36	100.0
Type of contact				
Negative	225	73.7	330	91.0
Doubtful	80	26.3	33	1
1 plus	305	100.0	363	100.0
2 plus	61		103	
Total	366		466	

P 0.001

The representativeness of the controls can be judged by comparison with Navy wide experience. The data in table 7 show the percentages of positive and doubtful reactors among recruits.

in the entire Navy and Marine Corps in the years 1949 to 1954. These figures were kindly supplied by Captain John F Chace, MC, USN. Applying each of these figures to the number of male

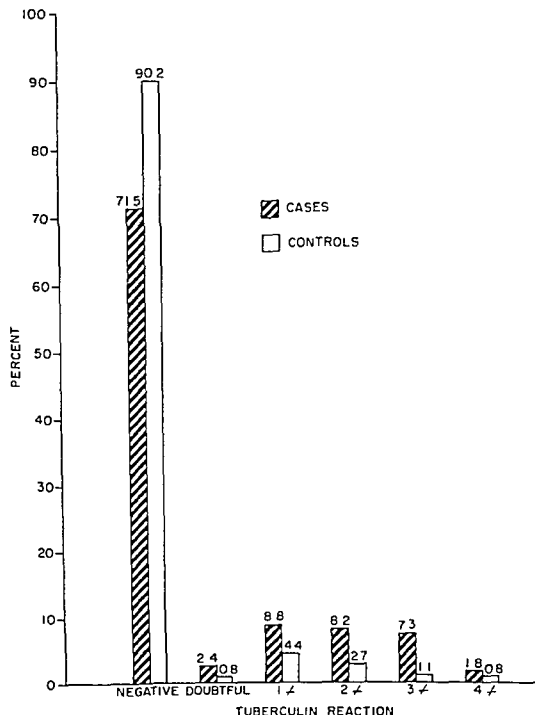


Fig. 1. Tuberculin sensitivity on first entry into service all personnel

enlisted controls who entered the service in the corresponding year, the expected number of reactors for that year and, by addition for the entire 6 year period, can be estimated. As table 8

show 6 controls were actually positive or doubtful reactors while 11 would be expected. This agreement is considered fairly satisfactory.

TABLE 7 *Incidence of tuberculosis in the U S Navy and Marine Corps 1949-1954*

Year	Positive (Percent)	Doubtful (Percent)	Total doubtful and positive (Percent)
1949	8.6	0.7	9.3
1950	11.1	0.7	11.8
1951	10.0	2.4	12.4
1952	10.0	2.4	12.4
1953	5.1	0.7	5.8
1954	4.5	0.8	5.3
Average (1949-1954)	8.8	1.7	10.5

TABLE 8 *Observed and predicted tuberculosis incidence in the U S Navy and Marine Corps 1949-1954*

Y ear	T b l e n y						T l Ob s r v d
	N		D b f l		P		
	Ob s r v d	Exp d	Ob s r v d	Exp d	Ob s r v d	Exp d	
1949	7	6	0		0		7
1950	63	62	0		7	8	70
1951	125	120	0	3	12	14	137
1952	96	95	3	3	9	11	108
1953	32	35	0		5	2	37
1954	7	7	0		0		7
T l	330	335	3	6	33	35	366

Table 9 presents the distribution of positive reactions according to the size and intensity of reactions for the study group, the controls, and the entire Navy and Marine Corps. Here again the controls resemble the entire service fairly closely.

TABLE 9 *Distribution of tuberculin test results in the U S Navy and Marine Corps 1949-1954*

Category	Reaction Percent				
	1 pl	2 pl	3 pl	4 pl	Total
Study group	33.6	31.4	28.0	7.0	100.0
Control group	48.5	30.3	12.9	9.1	100.0
Rest of U S Navy and Marine Corps 1949-1954 (Combined)	50.2	28.8	15.7	5.3	100.0

Comparison of the study group of cases with the controls (or equally well, with all service personnel recruited in the 6 year period) reveals two important differences (1) a much larger percentage of the cases were tuberculin positive at enlistment and (2) when only the positive reactions are examined, there is a considerable excess of 3 plus (strongly positive) reactions among the cases

It has been shown by Cornfield<sup>12</sup> that a comparison of the prevalence of an attribute in a case series with that in a control group can be made to yield an estimate of the relative incidence of the disease among persons in the population having, and those not having, the attribute. The validity of such an estimate depends on the extent to which the case series is representative of all cases of the disease in the population, and the control series is representative of the population itself. Reduced to its simplest form, the equation for deriving relative incidence of the disease from relative prevalence of the attribute may be expressed as follows

$$\frac{\text{Incidence among persons possessing the attribute}}{\text{Incidence among persons not possessing the attribute}} = \frac{p_1 q_2}{p_2 q_1}$$

where  $p_1$  and  $p_2$  represent the prevalence of the attribute (in this case, tuberculin sensitivity on entry to service) among the cases and controls, respectively and  $q_1$  and  $q_2$  represent the corresponding proportions of persons in the two groups who do not have this attribute. A condition for this equation is that the prevalence of the disease in the population must be small

In table 6, it is shown that of persons whose tuberculin status on entry was known, 28.5 per cent of cases and 9.8 per cent of controls were tuberculin positive or doubtful. If one considers only those (enlisted) personnel who had negative chest x-ray findings on entry into service, the proportion of tuberculin reactors is essentially the same, 26.3 per cent of cases and 9.1 per cent of controls. Hence the following values of  $p$  and  $q$  may be employed  $p_1$ , 26.3 per cent  $p_2$ , 9.1 per cent,  $q_1$ , 73.7 per cent, and  $q_2$ , 90.9 per cent.

These values, substituted in the above equation, lead to a rough estimate that the incidence of tuberculosis among tuberculin reactors was some 3.6 times that in the nonreactors. Unfortunately the reactions of 21 per cent of the subjects are unknown, a fact which lessens the confidence in the estimate.

It was originally hoped to find specific information as to the length of time initially negative tuberculin reactors served before conversion. Immunization records showed, however, that periodic tuberculin testing after entry was a rare event, even among medical department enlisted men. In regard to the latter, it is possible,



of course that local records of tests were not entered on the rhen s immunization registers. In any case the time intervals between initial and subsequent tuberculin tests were essentially those between entry into service and final diagnosis when tuberculin testing was again done.

In table 10 it is found that the median length of total service prior to coming under suspicion of tuberculosis was 28 months for the basic study group and 22 months for those of the study group who were tuberculin positive or doubtful on entry. This difference is significant and may be interpreted variously, one possibility being that some of the tuberculin positive men were recently infected or in the prodromal stages of active tuberculosis on entry. Navy or Marine Corps service perhaps hastening the appearance of clinical disease. Another possibility is that these men had healed lesions on entry which reactivated early in training. Since the controls were matched to the study group by length of service prior to diagnosis, their median falls between these values.

TABLE 10 Month of serv prior t susp t d gno by t bercul act on  
on entry t rvi f mal nl d per m l

M h f rv	C				C tr l	
	N ct		R ct		N	
	N mb	P	N mb	P	Numb	P
0-6	5	2.2	5	5.5	13	3.9
6-12	10	4.3	12	13.3	35	10.6
12-18	26	11.2	15	16.7	36	10.9
18-24	36	15.6	18	20.0	53	16.0
24-30	55	23.8	18	20.0	68	20.6
30-36	44	19.0	9	10.0	51	15.4
36-42	24	10.4	5	5.6	41	12.4
42-48	20	8.6	8	8.9	28	8.5
48 d	11	4.7	0	0.0	5	1.5
S bro l	231	100.0	90	100.0	330	100.0
U k wn	0		0		1	
T l	231		90		331	
M d (m h )	28		22		26	

The umb (36) f ct h l g p oo m l l t w r d strubut  
P < 0.001

The tuberculin status of men found to have nondisqualifying chest pathology on entry was investigated (table 11). It was noted that the term "tuberculosis" was rarely used in induction film reports of men who were accepted with nondisqualifying chest pathology. It might be anticipated that positive reactors would show more chest pathology (Ghon tubercles, et cetera) than non-reactors. The figures for both the study group and the controls are in accord with this expectation. There is also, unexpectedly, a small but significant excess in the percentage of initially tuberculin negative cases having x-ray findings "other than negative" on entry as compared to controls (3.0 per cent as against 0.3 per cent). A possible explanation for this difference is that a few men with chest pathology of tuberculous etiology were incorrectly read as negative reactors. Except for this, the correlation between tuberculin reaction and chest x-ray readings is in accord with expectation.

TABLE 11. Reactivity by tuberculin test results

Chest pathology	Negative				Positive				Total			
	C		I		C		I		C		I	
	N	P	N	P	N	P	N	P	N	P	N	P
Other	5	97.0	330	99	80	80.0	33	1.7	61	95.3	103	98.1
Sub	23	3.0	1	0.3	13	14.0	3	8.4	3	4.7		1.9
Unrec	1	100.0	331	100.0	93	100.0	30	100.0	64	100.0	105	100.0
Total	233		332		93		36		0		115	

are the percentages of men in the study and control groups who were born in the United States and who were born in other countries.

### Place of Birth, Residence, and Population of Residence

The degree of uniformity of state of birth and of given residence on entry into service was first examined for about 80 per cent of the persons in both groups; they were the same.

A comparison of cases and controls by region of birth, employing the grouping of states into nine geographic regions used by the U. S. Public Health Service in its morbidity reports, disclosed no striking difference in the origins of the two groups.

The percentage of positive or doubtful tuberculin reactions by region of residence of enlisted men in the United States was studied but the number of reactors was too small for meaningful findings.

The study and control groups were classified according to whether their place of residence at the time of entry into service was a community with a population under 2,500, between 2,500

and 50 000 or over 50 000 Table 12 suggests that an increasing percentage of the controls were tuberculin positive with increase in community size Since tuberculin status on entry has been shown to influence the probability of acquiring tuberculosis it was necessary to control this factor when studying the effect of community size Among nonreactors the proportions of study and control persons who came from small and large communities were closely similar In the case of positive reactors there was some difference but it was based on too small numbers to be meaningful

TABLE 1 Tuberculin sensitivity of control group by population size

Population	Number	Percent	
		Number	Percent
Less than 2 500	120	8	6.7
500 50 000	123	10	8.1
50 000 and over	124	17	13.7
Subtotal	367	35	9.5
Unknown	1	1	
Total	368	36	9.8

### Physical Characteristics

The heights and weights of all but three of the men under study were readily obtainable from accurate physical examination records made on first entry into service The distributions are recorded in tables 13 and 14 omitting the three unknowns

A comparison was made of heights and weights of the tuberculin negative control group with a sample of 565 tuberculin negative recruits processed through the U S Naval Training Station San Diego Calif in 1949-1951<sup>1</sup> The control group was slightly shorter than the San Diego group the medians being 68.7 and 69.2 inches respectively The weights were in closer agreement The San Diego group of course is less representative geographically than our control group since this Training Center draws recruits mainly from the western midwestern and southern sections of the country

The differences in height and weight between the basic study group and its control are noteworthy and suggest that tall men and thin men were more at risk of developing tuberculosis Again

TABLE 13 Height of entry into service — relative to deviation of weight from height standards

Height inches	Navy				Marine				Total			
	Standard		Control		Standard		Control		Standard		Control	
	N	%	N	%	N	%	N	%	N	%	N	%
60	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
61	0	0.0	1	0.4	0	0.0	0	0.0	0	0.0	1	0.9
62	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
63	5	2.7	5	2.0	0	0.0	4	5.1	5	2.7	9	3.6
64	6	3.3	10	4.0	0	0.0	1	1.3	6	4.8	11	6.9
65	5	2	22	8.7	2	4.3	7	9.0	7	9	29	15.7
66	12	6.6	21	8.3	5	10.9	7	9.0	17	15.3	28	24.2
67	17	9.3	41	16.2	7	13.0	8	10.2	23	5.4	4	39.0
68	25	13.7	40	15.8	11	23.9	13	16	36	41.2	53	55.0
69	31	17.0	29	11.0		15.2	15	19.2	38	57.9	43	68.0
70	26	14.3	25	9.9	4	8.7	10	12.8	30	71.1	35	78.6
71	25	13.7	24	9.5	7	15.2	9	11.5	32	85.1	33	68.6
72	16	8.8	16	6.3		4.3	2	2.6	18	93.0	18	91.0
73 in	14	7.7	18	7.1		4.3		6	16	100.0	20	100.0
Total	182	100.0	253	100.0	46	100.0	8	100.0	228	100.0	331	100.0
Mean (inches)	69.6		68.61		68.90		68.92		69.53		68.69	
Mean (inches)	69.10		68.34		68.74		68.19		69.06		68.30	
Standard deviation	2.60		2.81		2.13		2.41		2.52		2.72	
Standard error	193		177		315		272		167		149	

P &lt; 0.01

in comparing the percentage of deviation of weight from median weight for height standards on entry into service, a quite significant difference is noted in table 15 when all underweight categories are combined. The findings of these tables support the conclusion of Reed and Love<sup>14</sup> in their study of U. S. Army officers in 1933 that "The cases of pulmonary tuberculosis in young men are much more frequent among the thin ones, and especially the tall, thin ones." The same conclusion was reached by Long and Jablon<sup>15</sup> and by Palmer, et al.<sup>11</sup> Applying the formula  $\frac{P_1 Q_1}{P_2 Q_2}$

it may be estimated from the data in table 15 that the incidence among underweight men was 1.8 times that among normal weight and overweight men. Similarly, the incidence among men 69 inches tall or taller may be estimated at 1.7 times that among shorter men. Both estimates are valid only if the control group is representative of Navy and Marine Corps personnel. It is be

Table 1. Summary of findings of the study group

Group	Findings									
	Sex		Age		Race		Education		Occupation	
	Male	Female	White	Black	White	Black	High School	College	Professional	Other
Total	20	20	15	5	10	10	10	10	10	10
Mean										
Median										
Standard Deviation										
Range										
Correlation										
Significance										
Conclusion										

believed that the evidence of the present study is especially convincing in view of the limitation of the comparison to personnel tuberculin negative on entry.

Entries as to body build noted on induction physical examinations were tabulated to see if there was any correlation with deviation of weight from the median weight for height findings already presented. The correlation was poor because it was evident that examiners seldom used the descriptive terms heavy or obese even in cases of rather marked obesity. The evident misapplication of body build adjectives was too frequent to justify use of these data.

### History of Venereal Disease in Relation to Tuberculosis

A record of venereal disease while in military service is one index of close contact with civilians, often of low socioeconomic status, among whom the prevalence of tuberculosis is likely to be high. The material was therefore examined for evidence of correlation between tuberculosis and venereal disease. Seventeen per cent of the male enlisted basic study group had a record of urethritis or of penile lesions following admitted sexual exposure.

TABLE 15 *Percentage of deviation of weight from median weight for height standard on entry into service—male enlisted basic study group by service*

	Navy				Marine Corps				Total			
	Cases		Controls		Cases		Controls		Cases		Controls	
	No	%	No	%	No	%	No	%	No	%	No	%
Underweight	23	12.6	28	11.1	5	10.9	10	12.8	28	12.3	38	11.5
More than 15%	33	18.1	30	11.8	7	15.2	8	10.2	40	17.5	38	11.5
10-14%	44	24.2	41	16.2	13	28.3	17	21.8	57	25.0	58	17.5
5-9%	(100)	(54.9)	(99)	(39.1)	(25)	(54.4)	(35)	(44.8)	(125)	(54.8)	(134)	(40.5)
All underweight	60	33.0	84	33.2	14	30.4	24	30.8	74	32.4	108	32.6
Normal	22	12.1	70	27.7	7	15.2	19	24.4	29	12.7	89	26.9
Overweight	182	100.0	253	100.0	46	100.0	78	100.0	228	100.0	331	100.0
Subtotal	3		0		0		0		3		0	
Unknown	185		253		46		78		231		331	
Total												

$\chi^2 = 18.85$   
 $n = 2$   
 $P < 0.001$

In the comparable control group 15 per cent had a record of venereal infection, an insignificant difference.

### History of Contact with Tuberculosis

The induction medical history included questions as to familial history of tuberculosis but the reliability of the answer may be questioned. On the other hand the information from clinical records of the study and control group can hardly be contrasted since questions as to exposure would naturally be treated in history taking on a case of tuberculosis while on a case of appendicitis this point would receive much less attention. Consequently no comparison between the frequency of contact in case and control is justified. However we may contrast (table 16) the frequency of a history of contact, prior to service be-

TABLE 16. History of contact with tuberculosis prior to entry by venereal infection, by contact with tuberculosis prior to entry.

Record of contact	Tuberculosis		Tuberculosis	
	Number	Percent	Number	Percent
Study group				
Indication of contact	191	83.0	56	60
Other	1	9.6	25	(9)
		4	1	1.9
Total	230	100.0	81	100.0
Unknown	3		0	
Total	33		93	
Control group				
Indication of contact	95	96.4	30	85
Other	4	3.6	4	11.4
		1.3	1	2.8
Total	100	100.0	35	100.0
Unknown	6		1	
Total	33		36	

P < 0.01

P < 0.05

tween members of the study group who were tuberculin negative on entry and those who were tuberculin positive, and, similarly, the contact histories of tuberculin negative and tuberculin positive controls. Both comparisons reveal a higher frequency of contact among men whose tuberculin reactions were positive on entry. The majority of such recorded exposures were to persons in the immediate family. Among cases, familial contact was reported in 10 per cent of the tuberculin negatives and 27 per cent of the positives among controls, in 2 per cent of negatives and 11 per cent of positives. It is impossible to evaluate this information in the sense of estimating what proportion of tuberculous illnesses were acquired as a result of exposure in the patient's home either before or during military service, but some of them undoubtedly were.

The Navy's intensive program of searching out and examining all known close contacts of tuberculous servicemen is reflected in the fact that 31, or 13 per cent, of the basic study group of cases gave a history of in service contact with tuberculous service personnel.

### [To be concluded]

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# ESOPHAGEAL CORROSION BY ATTEMPTED SUICIDE IN THE ARMY

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**C**ORROSIVE substances are not often utilized in suicide attempts in this era the great majority of corrosive injuries being due to accidental ingestion. The amount of damage to be expected is worse when suicide is the intent because even though a spontaneous reflex tends to cause quick ejection of the material from the mouth and throat in spite of the person's intentions the subject bent on self injury is likely to gulp the first swallow. This is because he expects the material to be unpleasant and because there must always be a sudden last minute impulse to go ahead with the act. Another important difference between suicidal and accidental cases is that the former are adults while the latter are most often children.

This report deals with the study and treatment of 14 active duty Army personnel who attempted suicide through ingestion of a corrosive substance.

## THE PATIENTS

There were 11 men and three women in the group. Four were Negroes the others Caucasians. Five of the patients were between 18 and 21 years of age five were 22 to 26 years and one each was 35, 37, 49, and 58 years old. Three of the younger men attempted suicide just before Christmas and two on the day before their birthday. All but two of the other attempts were made in the early spring or late winter. Eight of the patients had been drinking prior to ingestion of the corrosive agent and it was believed that six of the eight had been drinking heavily. In each case it was concluded that a fairly serious attempt at self-destruction had been made. This is almost always the situation when agents of such generally recognized destructive effects are used for suicide.

## THE AGENTS

Eight of the patients chose household lye a mixture of sodium hydroxide and sodium carbonates for suicide four chose Drano which approximates household lye in its corrosive composition, and two used an Army issue cleaning compound composed of highly alkaline phosphates. Although it was often possible for the patient to indicate how much of the material he had taken into his mouth this did not give much information regarding the injury because expectoration, regurgitation, and vomiting had eliminated an unknown quantity after an unknown period of tissue contact.

## INITIAL CLINICAL FINDINGS

All patients were examined within 32 hours of the poisoning some within one hour. Five had had emergency first aid elsewhere. One patient was stuporous eight hours after having ingested household lye. The rest had severe pain in the mouth and throat. Odynophagia to the point of hydrophobia was encountered regularly. Deep substernal pain was a complaint of all and in some it persisted many days. There were no complaints of epigastric pain or discomfort elsewhere in the abdomen. Three patients had stridor on admission in one, this was severe enough to warrant an immediate tracheotomy.

Seven patients were vomiting blood upon admission and one who apparently had aspirated some of the corrosive material, had hemoptysis for 18 hours. A ninth patient first examined 32 hours after poisoning vomited copious amounts of pink orange pus without gross blood for 12 hours. Smears of the pus showed large numbers of square ended bacilli and cultures were positive for *Pseudomonas aeruginosa*. The other patients had ejected some of the corrosive and vomited briefly at the time of poisoning but did not vomit thereafter.

On initial oral examination maximum burn damage was found on the lips tongue soft palate and uvula. Irregular ulcerations with a gray filmlike slough were found within two hours of the poisoning. During the first two days these and the hyperemic appearance around the ulcerated areas changed very little except for gradual subsidence of underlying edema.

During the first 48 hours, all patients had some degree of fever. This reached a maximum of about 102°F in most cases. In two patients the fever lasted four days and in another six days.

Leucocytosis was a prominent laboratory finding. It usually persisted about a week. The highest count was 26 500 per  $\mu$ l, with 94 per cent neutrophils. The hemoglobin fell below 11 grams per 100 ml in nine patients but in all cases the esophageal

bleeding was brief and return to normal hemoglobin values was spontaneous and relatively rapid

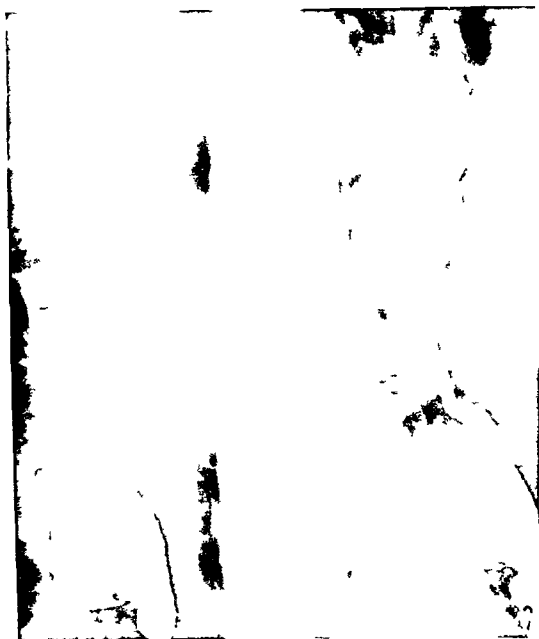
### PATHOLOGIC PROGRESSION

The progression of pathologic events within the esophagus was judged on the basis of serial roentgenographic esophagoscopic and transesophagoscopic biopsy studies which were continued at one to three week intervals as long as the patients remained under personal surveillance. Although initial examination seemed to indicate that mucosal injury had been produced throughout the esophagus in all cases the obscuring effects of edema, bleeding, and exudate production made accurate delineation of the areas of maximum damage very difficult early in the course (fig 1). After the acute reaction had cleared it was found that maximum injury had been sustained by the distal one third of the organ in three instances, by the middle one third in two, and by extensive scattered areas in the other nine.

The earliest endoscopic findings—on the third day—were constant from case to case. Regularly there was severe mucosal edema, sometimes softly occluding the esophageal lumen as a diffuse process, sometimes being irregularly distributed along the organ's length. Patchily spread over the paleness of the edematous areas were varying degrees of hyperemia, often intense. Necrotic, irregular, superficial ulcers occurred with variable frequency and severity from patient to patient. Although heavy and thin gray exudate was found regularly in cases in which no gross ulceration was observed, both exudate and blood were so prominent when ulceration was present that the esophagoscopic picture was one of strikingly angry, chaotic, almost amorphous tissue destruction. Biopsy specimens taken at this earliest stage showed coagulation necrosis, intense inflammatory necrosis, acute inflammatory exudate, and masses of bacilli. Tissue showed no cellular detail (fig 2).

At the end of the first week the only important changes found in the two patients re-examined this soon were disappearance of active bleeding and decrease in the amount of free exudate in the lumen. Biopsy specimens, however, revealed a strikingly intense acute inflammatory reaction with many bacteria in wholly necrotic surface tissue.

By the end of the second week esophagoscopic examination showed that a marked change had occurred in most cases. Now the mucosa was clean and two features dominated the scene. The areas previously ulcerated were now filled in with soft, dark orange granulations, and those areas in which the epithelium had remained intact now appeared thick, leathery, and dead white. Often in these cases the distal esophagus showed rather typical mild, nonspecific erosive esophagitis with tiny scattered



*Figure 1. Roentgenographic findings 10 days after poisoning. The severe distortion is due largely to edema and spasm. On the same day a No. 40 French dilator was passed without difficulty.*

erosions, a small amount of exudate and hyperemia. Biopsy specimens at this stage showed coagulation necrosis of residual mucosa with hypervascularity and acute inflammation beneath and typical granulation tissue with beginning fibrosis elsewhere.

From this point on the progression of events showed two predominant features: regression of inflammation and granulation and progression of fibrosis. From the third week through the third or fourth month, however, great variability was found from patient to patient in the rapidity of these changes. In one patient



*Fig. 2. Biopsy of loughed esophagus 1 month after poisoning (×110)*

successive biopsy specimens showed that granulation persisted for four months gradually being replaced thereafter by hypervascular fibrous tissue rich in fibroblasts. In other patients beginning fibrosis was evident histopathologically a week after poisoning.

Although in all patients dilatations prevented clinically important stricture formation during the period of observation a tendency to form strictures was observed regularly both roentgenologically and esophagoscopically. This was first encountered three weeks after poisoning as best the point could be

determined however the distinction between narrowing due to infiltration and edema and that due to actual stricture is not as easily made as one might guess. As time went on it became evident that multiple strictures were the threat. In some cases 10 or 12 areas of beginning stricturing could be identified. These areas of chronic repair for the most part corresponded to the areas of maximum acute injury. Some of the narrowings involved one half to two thirds of the length of the esophagus while others were short and weblike (fig. 3).



Fig. 3. Koontz roentgenographic findings eight weeks following poisoning. The distal one third of this esophagus was severely corroded. Extensive esophageal stricture is evident but the lumen remains adequate and at this point a 36 French dilator.

## TREATMENT

All patients were treated by a previously described modification of the Salzer technic. Steroid therapy was used in only one case with results already reported. Briefly, the technic calls for passage of a Levin tube into the stomach as soon as the patient is encountered, both to maintain an esophageal lumen and to permit hydration and feeding. On the third day the tube is withdrawn and esophagoscopy evaluation of the damage is made. Although this gives relatively little detailed information if the esophagus has been severely injured, it must be borne in mind that patients with severely burned mouths and throats may have sustained no esophageal injury at all—this is the point that early esophagoscopy examination must establish.

Immediately thereafter, daily dilatations are begun with Hurst mercury bougies, beginning with and if possible continuing with a bougie of large diameter, perhaps a No. 42 French. After about three weeks the dilatations are carried out at less frequent intervals (three times a week, then twice a week, once a week, et cetera), but the patient must be kept under medical surveillance for years. During the first three weeks large doses of penicillin and streptomycin are used, because secondary bacterial infection of the esophageal wall probably is as conducive as the corrosion itself to later fibrosis and stricture formation.

Although this is not an easy technic for patient or doctor, no special problems were met in this group of patients. It is particularly important to note that there were no complications from the transesophageal manipulations, for the technic has been criticized as dangerous. The most realistic danger is that of permitting strictures to develop. A conservative attitude which permits an esophagus to close off months or years later is reprehensible; an iatrogenic esophageal perforation in the course of sincere prophylactic ministrations is not.

The results of the present treatment could be judged personally over only relatively short periods, because after definitive treatment had been instituted the patients usually were transferred to a Veterans Administration hospital for the remainder of their course. Although personal observation averaged only seven months per patient, reports were received up to eight years in some cases. One patient died five months after the poisoning of pulmonary embolus from bilateral lower extremity thrombophlebitis.

All of the patients responded satisfactorily to dilatations, none requiring gastrostomy or other surgery. The problems encountered in keeping the esophageal lumen open, however, were very difficult in some patients. Passage of a No. 42 French

bougie on the fourth day following poisoning was very easy. Ordinarily no resistance was felt until about the tenth day. At that time it was common to find that suddenly the esophageal lumen seemed much narrower now able to accommodate only a bougie of much smaller caliber. In one typical case of severe esophageal damage the largest bougie which would pass through the entire length of the esophagus into the stomach from day to day from the fourth day on was as follows: No 42 French 42 42 36 40 40 30 30 36 36 40 40 30 32 32 32 32 30. In spite of loss of ground such as this it was believed that dilatations could be carried out less frequently from this point on both because biopsy studies show that the intramural pathologic processes have slowed down to a great extent by the beginning of the fourth week and because it has been found that less frequent dilatations at this stage are effective in producing a gradual enlargement and in maintaining an optimum lumen. Thus through the fourth, fifth, and sixth weeks in the case just cited the maximum sized bougie which could be passed on successive efforts was respectively No 32 36 36 42 36 36 38 42 French. The important thing is that dilatations, with periodic roentgen and endoscopic evaluation be continued indefinitely. The patients throughout the course of treatment are swallowing well and see no reason for continued dilatations. It is this asymptomatic phase which is so dangerous for fibrosis is gradually accumulating. The behavior of esophageal fibrosis is notably insidious in that following an insufficiently treated corrosive burn, stricture may not make itself known for many months or even years. Although as stated these patients were not followed personally to conclusion of their prophylactic dilatation therapy it was thought that they were headed toward good eventual esophageal function provided dilatations and periodic evaluation were studiously continued.

#### SUMMARY AND CONCLUSIONS

The clinical pathologic and therapeutic aspects of esophageal corrosion as they were observed in 14 active duty Army personnel who attempted suicide through ingestion of corrosive materials have been reported, with emphasis on the safety, apparent effectiveness and importance of early prophylactic dilatations.

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## CASE REPORTS

### Teratoma of the Thyroid Gland in an Infant

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**T**ERATOMAS of the thyroid gland are a rare finding. In a comprehensive review of the literature in 1935 Pusch and Nelson were able to find only 28 cases of thyroid teratomas occurring in the newborn and infants. Potter found that although teratomas of the thyroid are rare it is one of the more common tumors presenting in the newborn and frequently may produce dystocia or stillbirth. White and Gosselin and Bale reported on teratoma of the neck in the region of the thyroid gland; however these cases were not considered histologically as arising from the thyroid gland.

The purpose of this article is to present a case of teratoma of the thyroid gland detected in an infant and treated with good results.

#### CASE REPORT

The patient was a 2 year old male whose mother noted a small soft nontender mass in the anterior lower part of his neck about three months prior to his admission to this hospital on 25 April 1957. The mass had gradually increased in size. In retrospect the mother felt that the child's neck had always appeared fuller and thicker than she would have expected. The child had been noted to feed with difficulty on occasions and did not tolerate solid foods easily. He also had maintained a chronic course moist type of respiration which the mother had attributed to an upper respiratory allergic condition. There were no other significant findings or events as related by the parents.

Physical examination revealed no abnormal findings except for the presence of a firm rubbery nontender mass just to the right of the midline at the base of the neck. The mass measured 2 by 2 cm on palpation. The patient's respirations were of a rasping nasal quality. Urinalysis was negative. Blood cell count was within normal limits and the roentgenogram of the chest was normal.

On 26 April under general endotracheal anesthesia a low cervical collar incision was developed and the strap muscle divided. The mass was found to rest in the right thyroid fossa and was contiguous



*Figure 1 Photomicrograph of specimen showing the predominant features of the teratoma. Some of the cystic spaces are lined by glia and contain papillary projections ( $\times 10$ )*

with the thyroid isthmus. The left lobe of the thyroid gland was normal in appearance. The lesion appeared to be encapsulated and was removed with the isthmus. The posterior enlargement of the mass was found to cause pressure on the trachea and esophagus. The immediate postoperative course was uneventful.

On return to the surgical outpatient clinic the mother reported that the child's respirations were greatly improved and that his voice had lost its nasal quality. He was able to eat solid foods without difficulty and was experiencing no unusual symptoms. The patient continues

The child was started on Trilafon 4 mg three times a day. Approximately 24 hours later he was carried into the clinic rigid, unresponsive and appearing to be dead so that from his surroundings he had taken the third dose of Trilafon that morning prior to going to school and at school complained to his teacher of headache and stiff neck. Soon thereafter he was seen to start fixedly holding himself stiffly in his chair immobile.

Shortly after his parents brought him to the hospital the child was seen in neuropsychiatric consultation. He was lying rather rigidly on his side with one leg elevated in extension and without motion. His face was expressionless and he looked fixedly into space. There was no meningeal signs. His head could be bent forward and backward with the type of resistance designated as waxy flexibility. Motion of the child's extremities was productive of the same bizarre mobility. Releasing the extremities resulted in fixation in positions at levels in which they were released. There was no response to questioning and no outward show of pain. It was possible to move the patient into a sitting position; his head flexed back and his arms outstretched (fig. 1). Occasionally there was a Parkinsonian like twisting of the thumb. The neurologic examination including spinal fluid examination was otherwise negative. The appearance of the patient was best described as cataleptic, not unlike the picture of catatonics.



Fig. 1 (a) Child with fixedly extended arms and head tilted back.

Approximately three hours after admission the child began to respond by moving his extremities on command but otherwise continued to be uncommunicative. During the night brief episodes of torsion spasm were observed, but gradually these subsided and 16 hours after admission to the hospital he was entirely symptom free. His only remark in referring to his illness was "I was awfully afraid."

**Case 2** A 6-year-old girl was seen in the outpatient department of this hospital for an upper respiratory infection. She gave a history of "earache" approximately a week before during which she had a slight elevation in temperature and her mother had kept her from school. The day before her visit to the clinic she had returned to school but it had been necessary to send her home due to sudden onset of nausea, vomiting, and headache. At the clinic she was found to have a relatively mild upper respiratory infection. Because the nausea and vomiting continued, the patient was placed on Trilafon 4 mg three times a day. The following day, after three doses of the medication, the patient complained of pain in the back of her neck, drawing her neck back. According to the mother, her face pulled to one side. She "stiffened" and was brought to the hospital relatively immobile, speechless, and presenting the same picture as outlined in the previous case. She was seen in neuropsychiatric consultation and in addition to the above, the following history was elicited. She is the second of three children. Birth and development were outlined as normal. She is in first grade and, according to the mother, "she is the teacher's pet." Two weeks prior to admission, the child saw her father, who had been overseas, for the first time in seven months. He was home only for the night and was due to return home the night of the child's admission to the hospital. The child allegedly had missed her father greatly and had crying spells about his being away. When the child started vomiting the morning of her initial visit to the clinic, the mother thought it was a case of excitement related to the fact that father would be home the following night. The mother described her daughter as highstrung and sensitive but with the sweetest disposition.

Neurologic examination findings were essentially the same as in case 1. The child had a fixed stare, her features were immobile but did not express pain. The same "waxy flexibility" was elicited in all the extremities and in the neck. It was possible to sit the child upright and move her arms and legs to positions held without further motion. The neck tended to pull backward as though in spasm (fig. 2) yet it was possible to bend it fully forward and backward without eliciting any demonstration of pain. All indicated studies, including spinal fluid examination, were within normal limits. She remained immobile with extremities in a semirigid position and with head pulled to one side for about four hours after her admission to the hospital. After this she gradually relaxed and on command was able to move her extremities and to change her position in bed. Several hours later she became relaxed, fell asleep, and was discharged symptom free the day following her admission to the hospital.

### CAREER PROGRAMS

That the residency training programs furnish a major initial incentive for transfer to the regular Medical Corps of the U S Navy is evidenced by the fact that the majority of officers accepting such commissions during the past few years did so for the purpose of being assigned to those programs. Indications now point increasingly to the likelihood of a good majority of these men making a career for themselves in the Medical Department of the Navy. It will be a very happy and fortunate circumstance indeed if this pattern continues to prevail for the so called Doctors Draft Law is just as unpopular with military authorities as with their civilian counterparts and with the profession of medicine at large in the United States. The only remedy for this difficult and trying situation is a potent nucleus of career medical officers. The Medical Department of the U S Navy as well as of the U S Army and the U S Air Force are urgently in need of the positive assistance and staunch support of all civilian physicians throughout the United States for the purpose of attracting a sufficient number of physicians to careers in military medicine to fulfill the critical responsibilities called for in our Constitution and in the Public Laws of the Congress. The potential catastrophic consequences of enemy thermonuclear biological and chemical warfare attack render it absolutely imperative that medical professional societies, organizations, institutions and individuals everywhere in the country come forth with positive programs of action to help the Medical Departments of the U S Navy and her sister services accomplish their cardinal missions. The new Public Laws of the 84th Congress relating to military career incentives, dependent medical care and survivors benefits including Social Security all should attract more physicians to electing the military as a financially sustaining professionally rewarding and wholesome career.

—ROBERT B. BROWN, Cpt MC USN  
MALCOLM W. ARNOLD, Cpt MC USN  
*A b of Surgery*  
p 252 Aug 1957

## Departments

### ARMY MEDICAL RESEARCH ADVISORY GROUP HOLDS FIRST 1958 MEETING IN WASHINGTON

The Advisory Council on Research Affairs to the Surgeon General of the Army Major General Silas B Hays held its first 1958 meeting in Washington on 21 and 22 March Brigadier General Perrin H Long MC USAR Chairman of the Department of Medicine Down-Statc Medical Center State University of New York presided at the conference which was attended by 8 members of the 11 man group

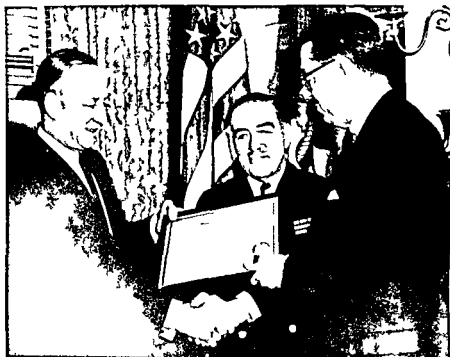


*Seated (left to right) Brigadier General Perrin H Long MC USAR and Major General Silas B Hays MC USA standing Brigadier Generals Frank E Wilson James B Mason Manfred U Pescotti Harold C Lueth Truman G Blocke J Carl S Junkermann and Joseph M Bosworth MC USAR*

Following the meeting Brigadier Generals Alexander Marble MC USAR Professor of Clinical Medicine Harvard University School of Medicine and Harold G Scheie MC USAR Professor of Ophthalmology University of Pennsylvania School of Medicine departed for two weeks active duty training at the Brooke Army Medical Center San Antonio Tex They will attend a special course in administration of a reserve hospital center

## NAVY'S CERTIFICATE OF MERIT GIVEN FOR SERVICE IN HEALTH AND SAFETY

One of the Navy Department's high st c v l i a n awards the Cer t f i c a t e of Merit was present d to the CIBA Pharmaceutical Company recently in a ceremony in Washington. Represent ng the Secretary of the Navy Assistant S c r e t a r y F r d A B a n t z presented the c r t i f c a t e to Mr T F D a v i s H a i n e s president of the CIBA Company for out standing service to the Navy D e p a r t m e n t in the fields of h e a l t h and safety.



A s s i s t a n t S e c r e t a r y of the Navy F r d A B a n t z (l f t) R e a r A d m i r a l B a r t h o l o m e w W H a g a n and M r T F D a v i s H a i n e s

During the c e r e m o n y Secretary Bantz c o m m e n t e d on the exceptional service t h a t the CIBA Pharmaceutical Company has r e n d e r e d to m e d i c i n e and to the p o p l e of the U n i t e d S t a t e s in s p o n s o r i n g one of t h e v e r s i o n s n o t a b l e d u c a t i o n a l s e r i e s M e d i c a l H o r i z o n s

The c e r t f i c a t e c o n t a i n e d the following c i t a t i o n

F o r t h e d i s t i n g u i s h e d D e p a r t m e n t f i e l d f h i l h  
a n d s a f e t y A p p o i n t m e n t f o r t h e p r o g r a m M e d i c a l S e r v i c e  
f o r t h e U n i t e d S t a t e s H e a l t h C o m m i s s i o n C I B A C o m p a n y b y g h g t d t  
t h e N a v y a d M e d i c a l C o r p o r a t i o n t o t h e U S

Naval Submarine Base New London Connecticut depicted an unusual facet of the work of the Navy Medical Corps in showing how the health and safety of Naval personnel engaged in underwater activities is under constant medical observation. The nature of the story material served to inform the public that certain hazards are associated with the rapidly growing sport of scuba diving and conveyed to the medical profession the nature of casualties and appropriate treatment as well as measures of prevention.

Also present at the ceremony were Rear Admiral Bartholomew W. Hogan MC USN the Surgeon General of the Navy other officials of the CIBA Company representatives from the Bureau of Medicine and Surgery Department of the Navy Washington D C and the U S Submarine Base New London Connecticut and civilian physicians from the Washington area.

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## CAPT HOUGHTON NAMED NAVY CHIEF NURSE

Captain Ruth A. Houghton NC USN succeeded Captain W. Leona Jackson NC USN as Director of the Navy Nurse Corps 1 May.

Born in Andover Mass. Captain Houghton was graduated from the St. John's Hospital School of Nursing Lowell Mass. and received her Bachelor of Science in Nursing Education from Boston College. She has completed her work for the degree of Master of Science at Catholic University. She entered the Nurse Corps on 1 June 1935 and was appointed captain on 17 October 1957. She is a member of the American Nurses Association the National League for Nursing the Association of Military Surgeons Sigma Theta Tau and Pi Gamma Mu.



*Captain Houghton*

Captain Jackson retired on 30 April after a four year assignment as Director of the Nurse Corps.

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## DEATH

HURST Charles Wesley Lieutenant Colonel 1 MSC USAR of McKay Idaho stationed at Letterman Army Hospital San Francisco Calif. served in an enlisted status in the United States Army from 4 March 1931 until 3 September 1934 commissioned in the United States Army Reserve 21 August 1938 ordered to active duty 26 September 1940 died 8 February 1958 at 43 at Colma Calif. of a self-inflicted gunshot wound.



## POSTGRADUATE PROFESSIONAL COURSES OFFERED ARMY MEDICAL SERVICE OFFICERS

The following Postgraduate Professional Short Courses for Army Medical Service Officers are announced for the first quarter Fiscal Year 1959. Persons interested and eligible to attend should apply through channels to The Surgeon General, Department of the Army, Washington 25, D. C. Attention: MEDCM CG.

Ad d M l t y P t M d i —W l R d Army In f R-  
h 14 J ly 18 O b 1958

This course is designed to supplement the training given Army officers at civilian schools of public health by giving instruction in those aspects of preventive medicine and hygiene that are peculiar to the Armed Forces. A prerequisite is a master's degree in public health or its equivalent granted by a recognized civilian institution and enrollment is restricted to officers continuing their careers in either preventive medicine or staff and command. Although the course is primarily designed for medical dental or veterinary officers, engineers, entomologists, and nurses who fulfill the entrance requirements will be accepted.

R d t p i M d —W l R d Army In t t f R h 14 July 10  
O b 1958

This course consists of three months of training in mathematics, physics, laboratory techniques, and theory of diagnosis and therapy involving radioactive materials. The students will be required to take a refresher course in general physics and nuclear physics as well as the applicable mathematics involving problem work. The theory of radioisotopes in medicine will be combined with actual patient contact at the radioisotope clinic. The course is designed to qualify medical officers in the use of radioisotopes in order to meet the requirements of the Atomic Energy Commission and for authorization for handling radioisotope classes in Class I and Class II installations.

M g m t f M C l t —W l t R d Army I f R h  
15 20 Sept mb 1958 B k Army M d c l C 28 J ly 1 A g 1958  
d 22 6 S p mb 1958

The purpose of the course is to indoctrinate officers of the military medical services in current concepts on the management of casualties resulting from the employment of nuclear weapons. The course is designed to provide current up-to-date information of an unclassified nature on the medical aspects of nuclear warfare to reduce the information to a level accessible and useful data in the solution of problems that might arise and to stimulate thinking on ways of coping with the problem of casualties which might result from nuclear weapons.

Eleventh Symposium on Pulmonary Disease—Fitzsimons Army Hospital  
8-12 September 1958

The Eleventh Annual Symposium on Pulmonary Diseases will cover the diagnosis and treatment of tuberculous and non-tuberculous diseases of the chest. Material will be presented in lectures, live clinics and demonstrations with emphasis on case presentations to small groups of participants. Demonstrations of techniques of pulmonary function, bacteriologic methods, physical medicine, chest surgery et cetera will be provided.

Pulmonary Function Testing as Applied to Disability Ratings—Fitzsimons Army Hospital 13 September 1958

This course is divided into afternoon and morning sessions. The morning session will be conducted in the laboratory with discussion of equipment and methods and demonstration of testing techniques. Pulmonary function testing to be covered will be limited to the clinical type procedures to include external spirometer measurements of flow rates, measurement of lung volumes and lung compartment relationships (open circuit nitrogen washout and closed circuit helium dilution), exercise measurements of ventilation and oxygen utilization (the work of breathing), oximetry (continuous recording type) and arterial blood gases (technic of Van Slyke measurements and pH determinations—Beckman Model G with special blood electrode).

The afternoon session will be devoted to a panel discussion on the use of physiologic tests in profiling disability in cardiopulmonary diseases. It will center around specific case presentations that illustrate various categories of pulmonary insufficiency and related disability. The cases will be selected from the pulmonary function clinic, Fitzsimons Army Hospital.

Medical Nursing—Walter Reed Army Institute of Research 22-27 September 1958

This course is designed to provide an opportunity for nurses to appraise and plan for the needs of patients in the medical service for comprehensive nursing care applicable in Army situations. Emphasis will be placed on recent developments and trends in the clinical aspects of medical care and treatment of patients with selected disease conditions such as cardiovascular disease, endocrine disturbances, gastrointestinal disorders, communicable diseases, degenerative diseases et cetera. In considering optimum nursing care for patients with these disease conditions, a portion of the time will also be devoted to the multidisciplinary approach to care of patients and nursing team concepts, priority of care, continuing need for in-service education and on-the-job training, and implication for study and research to improve nursing care of medical patients.

Principles of Medical Operations in Nuclear Warfare—Walter Reed Army Institute of Research 29 September-31 October 1958

This course is designed to teach selected medical officers the principles involved in medical operation in nuclear warfare to include a review of mathematics and theory nuclear weapons systems phenomenology and human effects and medical plans training and applications

C o u r s e     L e c t u r e     — W a l t e r R e e d A r m y I n s t i t u t e  
R e s e a r c h     S p r i n g     1958

This course will present to Medical Service Corps laboratory officers recent advances in method and the interpretation of results in biochemistry bacteriology serology medical zoology virology and hematology. This will be augmented by an introduction to laboratory automation. In addition certain aspects of atomic casualty studies of particular interest to the laboratory scientist will be presented. For the most part the material will be presented by the lecture demonstration method. The student also will have an opportunity to acquaint himself with the techniques of individual tests. The laboratories of Walter Reed Army Medical Center also will be available for consultation on individual problems.

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## OFFICIAL DECORATIONS

The following awards were recently announced by the Departments of the Army and Air Force

### Legion of Merit

H e n r y G. A.     J. M. J. G.     USAF (MC)     J. H. H. W. L.     C. I. USAF (MC)  
J. E. K.     B. K. M. J. G.     USAF (DC)

### Commendation Ribbon

H. M. C. K. W. L.     C. P. M. C. USA

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S. J. O. K. L. F. C. I.

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## First U S Meeting of WHO Begins 28 May

The World Health Assembly, the governing body of the World Health Organization, will hold its eleventh session in Minneapolis, Minnesota, beginning on 28 May 1958 and continuing for a period of three weeks. The United States will be host for this meeting, which will mark the tenth anniversary of the WHO and the first time the delegates of the United Nations have held their deliberations in this country.

Dr. S. bin Hass, Al-Watbi, former Minister of Health of Iraq, who was last year president of the World Health Assembly, will open the 1958 session and preside until his successor is elected. Dr. M. G. C. and U. S. Director General of WHO.

## A MESSAGE FROM THE A M A

This is the second and concluding part of a report on the results of a continuing opinion survey of physicians released from active military service. The first part of this report appeared in last month's issue of the *U S Armed Forces Medical Journal*. This summary is based on 1 600 returns received in 1956. A total of 2 519 questionnaires were distributed by the Council on National Defense of the American Medical Association.

**Physicians' Evaluation of Staffing Conditions** One of the questions was designed to obtain the opinion of physicians as to staffing conditions of nurses, enlisted medical personnel, physicians, dentists, and others at the two units where the physician served his longest and next longest assignments. With respect to the longest assignment, the tabulation of this multiple answer question indicated that in the Army, replies of overstaffing totaled 691, understaffing 823, and adequate staffing 1 470. In the Navy, overstaffing totaled 738, understaffing, 811, and adequate staffing, 1 415. The Air Force tabulation revealed 461 replies of overstaffing, 636 of understaffing, and 819 of adequate staffing. The response to the question concerning the next longest assignment revealed that in the Army, overstaffing totaled 671, understaffing 701, and adequate staffing 1 174. In the Navy, the results were 697, 702, and 1 243, respectively, while the Air Force tabulation was 414, 473, and 710, respectively. Physician overstaffing in the Army and Navy and dentist overstaffing in the Air Force predominated in regard to the longest assignment, while physician overstaffing led in all three services with respect to the next longest assignment. On the longest assignment, dentists and enlisted medical personnel were second and third, respectively, in regard to overstaffing in both Army and Navy, while physicians and enlisted medical personnel were second and third in the Air Force. On the next longest assignment, dentists and enlisted medical personnel were second and third, respectively, in the Army and Air Force, while enlisted medical personnel and dentists were second and third in the Navy.

**Unnecessary Aspects of Military Training** There were 477 physicians who responded affirmatively to the question "Were there any aspects of your military training that were unnecessary or wasted?" Negative answers were received from 1 120 medical officers. Of those who answered affirmatively, the majority were of the opinion that nonmedical duties was the area of greatest waste in their military training. In the Army, 74 per

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From the Council on National Defense of the American Medical Association. The views and opinions expressed are not necessarily those of the Department of Defense.  
—Editor

cent of those who responded affirmatively were of that opinion as were 37 per cent of those in the Navy and 73 per cent of those in the Air Force

**Making Military Service More Attractive** A total of 1476 physicians offered suggestion for making military service more attractive for the practice of medicine Only 124 physicians thought that nothing could be done to make military service more attractive to medical men The leading suggestion of physicians in all three branches of the service was that there be an improved utilization of medical personnel An increase in pay was the second most frequent suggestion from physicians in all branches while higher rank with merit promotions was third as the suggestion of Army physicians choice of stable location was third for the Navy and more capable commanding officers was third for the Air Force

**Improvement of Services to Military Physicians by Medical Associations** A total of 515 physicians (32 per cent) offered suggestions in response to the question concerning the role of national and local medical associations in maintaining closer contact or rendering better service to their members who served as physicians in the Armed Forces The other 1082 physicians who returned the questionnaire offered no suggestions The most frequently suggested improvements in services were (1) more personal visits by civilian physicians to evaluate grievances (2) more invitations to military physicians to civilian medical meetings and (3) the dissemination of more information to military physicians

**Physicians Who Would Voluntarily Remain in Service** In response to the question relative to military service beyond the obligated tour of duty 929 physicians indicated they would not be willing to stay in military service for more than two years under any conditions except total war There were 671 physicians who indicated they would serve an additional period under certain conditions Many physicians listed more than one condition The most frequently listed condition was "increase in pay" followed by choice of stable location choice of duty assignment and opportunity to practice specialty

**Preferred Branch of Service for Practice of Medicine** There were 608 physicians who stated a preference for the Armed Forces in response to the question of preference if the physician were going to practice medicine in a Federal Government agency A total of 971 physicians expressed a preference for other agencies of the Federal Government while 18 physicians had no preference Of those who preferred the Armed Forces the vast majority chose the branch of service in which they had served



## NAVY SCIENTIST GIVEN HIGH CIVILIAN AWARD

Doctor Clay G. Huff, head of the Division of Parasitology in the Naval Medical Research Institute, Bethesda, Md., recently was awarded the Navy Distinguished Civilian Award at ceremonies in the Office of the Assistant Secretary of the Navy, Fred A. Bantz, for contributions in the field of parasitology, especially the malarial parasite during the past 30 years.



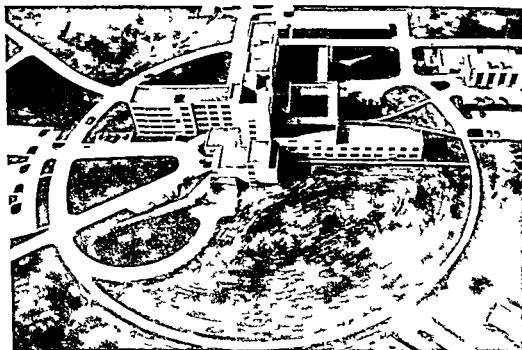
Assistant Secretary of the Navy Fred A. Bantz, Director Huff, Rear Admiral Bruce E. Badley, MC, USN, Deputy Surgeon General of the Navy, and Captain Ott E. Van Dusen, MC, USN, Commanding Officer, Naval Medical Research Institute.

Dr. Huff formerly was professor of parasitology at the University of Chicago. Since joining the Institute in 1947, his achievements have brought him recognition in the form of offices in several professional societies and the Theobald Smith Gold Medal awarded by the American Academy of Tropical Medicine for outstanding work in tropical medicine.

## NEW HOSPITAL AT FORT RILEY NAMED FOR GEN JOHN IRWIN "THE FIGHTING DOCTOR"

The new Irwin Army Hospital Fort Riley, Kans. named in honor of Brigadier General Bernard John Dowling Irwin "the fighting doctor" and early winner of the Medal of Honor was dedicated in an appropriate ceremony on 7 February 1958. Major General Silas B. Hays, Surgeon General of the Army, was the principal speaker.

Constructed in the latest military design at a cost of more than five million dollars, the new hospital is the third to be completed in the Army's program of modern medical facilities. The main building consists of five structurally separated units designed to provide medical service for 250 bed patients. It is expandable to a capacity of 500 beds by the construction of additional ward wings. The commanding officer is Colonel Milford T. Kubin, MC, USA.



*Irwin Army Hospital Fort Riley Kansas*

The late General Irwin was born in Ireland on 24 June 1830 and received the degree of doctor of medicine from the New York Medical College. In 1856 he was commissioned in the Army medical service and served in New Mexico and Arizona. In an engagement with the Chiricahua Indians near Apache Pass, Ariz. in February 1861 he commanded detachments of Companies C and H, Seventh Infantry and subsequently received the Medal of Honor for gallantry in action. He was post surgeon of Fort Riley on two occasions between 1866 and 1873. He was appointed Assistant Surgeon General of the Army in July 1892 and retired two years later. He died in 1917.



## Reviews of Recent Books

CLINICAL HEART DISEASE by *S m l A. Lev* M D F A C P 5th  
d t 673 p g ill t ted W B S und C Phil d lphia P  
1958 P \$9

The author is a colorful well known clinician and teacher who has not changed his purpose and goal in this fifth edition. He attempts to present the important aspects of diagnosis prognosis and treatment of heart disease in a simple manner aimed primarily for the general practitioner. It is written in a narrative style in the first person with many references to clinical cases as if he were conducting a teaching conference. There is no bibliography.

This book has 22 chapters each being a brief treatise on the subject under discussion. It was not intended to be comprehensive in scope or in detail. The chapter covering congenital heart disease was written by Dr Alexander Nadas who is an outstanding authority in this field. The chapter on electrocardiography covers 232 pages and was written by Dr Harold D Levine. A general introduction to vectorcardiography is incorporated into this chapter.

This book has many good features in the realm of clinical observation and general management of heart disease. There also are several drawbacks to this book. There is a tendency toward verbosity and rambling. While there is a great deal of excellent information in this volume it is not organized for quick reference or review of the material.

The author discusses various elements of diagnosis prognosis and treatment in a general way but this is not considered comprehensive enough for the serious student of internal medicine or heart disease. —DOSSO LYNN C L MC USA

THE YEAR BOOK OF OBSTETRICS AND GYNECOLOGY (1957-1958 Year  
Book Series) edited by *J P G* h ill B S M D F A C S  
F I C S (Hary) 597 p g ill tr t d Th Y ar B ok P b-  
l h r I Ch c g ill 1957 P \$7.50

This pocket size book is composed entirely of articles abstracted from journals published between July 1956 and July 1957. It is a comprehensive review of the literature covering that period and edited by a noted authority in the field. However, no mention is made to the criteria used in selecting an article for inclusion. It must therefore be assumed that articles are included simply on the basis of their appearance in the literature during the time covered by the book. No attempt is made to evaluate the articles abstracted. In fact, the editor's notes consist of additional abstracts which in most instances do not bear on the previous article but deal instead with a different phase of the subject discussed. This criticism can of course be rendered impotent if the book is intended as a reference rather than a text. If the intention is that of a reference then its value is in question from another quarter, namely duplication of effort. Her

the reviewer makes reference to the fact that other publications are in existence with the same purpose. The busy practitioner no doubt prefers less duplication of effort by such authorities as J P Greenhill and more guidance to the valuable articles published so reading time can be used most wisely —J WILSON HUSTON Capt MC USN

**ADVANCES IN RADIOBIOLOGY** Proceedings of the Fifth International Conference on Radiobiology held in Stockholm on 15-19 August 1956 edited by *George Carl de Hevesy*, *Arne Gunnar Forssberg* and *John D Abbatt* 503 pages illustrated Charles C Thomas Publisher Springfield Ill 1957 Price \$15.50

This volume consists of 69 papers and covers the broad field of radiobiology including fundamental effects at the cellular level, general physiology including hematology and genetics. A large section more than one fourth of the papers is concerned with the exciting new leads and modification of systemic radiation effects including an exposition of the general principles, chemical methods and the bone marrow work which has recently received much publicity. As in previous years a number of reports have direct application for the clinical radiologist. These include isotope studies as well as problems with leukemia. In a particularly interesting paper Lounit reviews Kaplan's leukemia hypothesis as proposed in 1954 and a preliminary report by Faber from Denmark confirms earlier presumptive evidence of the association between clinical radiation exposure and leukemia.

The book is dedicated to H J Muller and contains 10 papers covering recent work in the field of genetics including some human implications by T C Carter. The principles of back mutation as well as modification in recovery from chromosomal damage are discussed. The nature of the proceedings are broad enough to be valuable to the clinician interested in radiotherapy and the treatment of cancer and to the hematologist, radiation chemist and radiobiologist.

—JAMES B HARTGERING Lt Col MC USA

**CARDIOVASCULAR REHABILITATION** edited by *Paul Dudley White* M D, *Howard A Rusk* M D, *Bryan Williams* M D and *Philip R Lee* M D 155 pages The Blakiston Division McGraw-Hill Book Co Inc New York N Y 1957 Price \$6.50

This book is an edited publication of the proceedings of a conference on cardiovascular rehabilitation conducted under the sponsorship of the Institute of Physical Medicine and Rehabilitation of the New York University Medical Center. Thirty-five authorities in the specialties of cardiology, industrial medicine, physical medicine and rehabilitation participated in the conference and their views on the important aspects of cardiovascular rehabilitation are presented in an informal manner.

Work physiology, critiques of the various tests of evaluating cardiovascular work and the physical, emotional and environmental aspects of work as pertain to the cardiac patient are well presented. The

functions of work classification units and of State and Federal rehabilitation services are briefly summarized. Problems in the field of rehabilitation uncovered in the early discussions are then related to requirements for the teaching of cardiovascular rehabilitation and emphasis is placed on those areas of present and future research that should be explored more fully. Of added value is the inclusion in the text of a comprehensive reference bibliography.

This timely, concise yet comprehensive text is of definite value and will clarify for the reader the important problems of rehabilitation and management of the cardiovascular patient that are so often neglected in the usual texts. Its value is not limited to the industrial health specialist or cardiologist; rather its worth is equally applicable to those in all the fields of medicine.

—LOREN F. PARMLEY, J. Lic. MC USA

THE PRINCIPLES AND PRACTICE OF DIATHERMY by Bryan O. Scott  
M. R. C. S. L. R. C. P. D. Phys. M. D. 193 p. g. Ill. t. t. d. Charl.  
C. Th. m. P. bl. h. Spn. g. f. Id. Ill. 1957 P. c. \$5

For physical therapists and others who require a clear and concise text on the fundamentals of short wave diathermy, this volume is valuable. The physics of this method of deep-heat therapy are clearly and comprehensively covered. The author wisely limits the content to the technical aspect of application and does not attempt to delineate pathologic conditions amenable to short wave diathermy. Included in this work are 18 chapters. The longest and voted technique concerning the regional application of the method of treatment. This reviewer has observed that this is a poorly understood subject but a noteworthy contribution has been made here. The many illustrations and diagrams are valuable and the simple explanations of technical terms make for lucidity and objectivity. Teachers of physical therapy will find this short volume ideal as a textbook for students who are seeking to acquire basic facts on short wave diathermy.

—BENJAMIN A. STRICKLAND, J. C. I. USAF (MC)

THE RELATION OF PSYCHIATRY TO PHARMACOLOGY by Abraham  
W. K. M. D. 322 p. g. P. bl. h. d. fo. th. Am. c. S. ty. f. r.  
Ph. m. l. gy. d. E. p. m. t. l. Th. p. t. by Th. W. l. l. a. m. d.  
W. l. k. C. B. l. m. M. d. 1957 P. r. \$4

This book is a review in which an attempt has been made to survey the literature from 1930 to 1955 for material dealing with the effects of drugs used in psychiatry in the treatment or investigation of the functional behavioral disorders. This is an immense task and as the author points out, the present review may be regarded only as an attempt to survey the problems which will have to be resolved in the future. The drugs reviewed are limited primarily to insulin, carbon dioxide, barbiturates, amphetamine and methamphetamine, piperidol, chlorpromazine, trisopine, meprobamate, et cetera. The book is divided

into two sections one on the Effects of Drugs on Human Behavior and the second on Theories and Mechanisms of Drug Actions Some repetition of material occurs in these two sections but this adds to the value of the review

For so difficult and complex a subject the author has prepared a well organized and easily read review and he has included in one book much of the important work in this field An adequate index adds to the usefulness of the book —SAMUEL V THOMPSON Capt MC USN

**PRACTICAL ALLERGY** by M Coleman Harris M D F A C P and Norman Shure M D F A C P 471 pages illustrated F A Davis Co Philadelphia Pa 1957 Price \$7 50

The authors have achieved a noteworthy accomplishment namely that of writing a book which fits the title perfectly Material is presented in a manner that makes it easy to assimilate and utilize in the ordinary practice of medicine and the practice of allergy by the nonallergist as well as the specialist in this field Just the right amount of theory and controversial material is presented to indicate just how little is known in allergy yet how much we can do for our patients despite this

A good portion of the book is directed at the details of completing skin tests desensitization technics and specific and nonspecific therapy In a book of this size it is impossible to be all inclusive and great detail in theory is not indulged in but the material is covered in sufficient degree to be useful and informative

This book is intended for the general practitioner and the nonallergist internist who thinks he would like to practice allergy It should assist materially in this endeavor —DAVID L. DEUTSCH Lt Col MC USA

**AN ATLAS OF FETAL AND NEONATAL HISTOLOGY** by Marie A Valdes Dapena, B S M D Foreword by Edith L Potter M D 200 pages illustrated J B Lippincott Co Philadelphia Pa 1957 Price \$11

This small atlas consists of a series of photomicrographs detailing the changing histologic structure of organs during fetal and early infancy All of the illustrations are in black and white In most instances there is sufficient detail to be useful to the pathologist and the student as a reference for normal structures The pattern of the book has a descriptive text on the left hand page with the photographs on the right This form is more difficult for quick reference than for example the section on the kidney which has the caption for the data under each photograph An excellent bibliography accompanies each section The book suffers from the lack of an index and it is somewhat awkward to use until one becomes familiar with its contents Pathologists and histologists should find this atlas a useful reference guide in the complexities of the normal histology of the developing fetus and the neonatal period —FRANK M TOWNSEND Col USAF (MC)

## ROENTGEN DIAGNOSIS OF ABDOMINAL TUMORS IN CHILDHOOD by

Ch l s M. N c J M D Ph D Al x der R M g l s M D  
d L C R g l r M D 75 p g Il tr r d Ch l s C Th m  
P bl h Sp g f ld, Ill 1957 P \$4

Dr Rigler and his fellow workers from the University of Minnesota Medical School make a worthwhile contribution to the field of roentgen diagnosis by stressing the importance of making an accurate pre operative diagnosis in cases of children with abdominal tumors. He states that a large number of such masses may be accurately evaluated by relatively simple clinical and roentgenologic methods using a minimum of manipulation and expenditure of time and affording the child much benefit and little harm.

The monograph discusses the importance of topographic location of masses in the abdomen and means of localizing such masses. The various landmarks and their displacements are described and a roentgen classification is offered. Their relative incidence in childhood and infancy is discussed.

The 75 page volume is beautifully illustrated by line drawings of body sections and schematic presentations as well as excellent reproductions of radiographs with plain films and using contrast materials showing various displacements by tumors. A comprehensive bibliography is included for those wishing to continue the subject. The book is highly recommended especially as a teaching aid for radiologists, oncologists, pediatricians, surgeons, and general practitioners who may deal with children. —SYLVESTER F WILLIAMS Capt MC USN

TUBERCULOSIS E ry Ph y n P bl m by J A th Myer M D  
290 p g Il tr ted Charl C Th m P bl h Springf ld  
Ill 1957 P c \$7.50

This book was written for physicians in every phase of medical practice and covers the subject broadly. It is very readable and presents the material in a personal manner. While other authors are freely quoted they all not unnaturally seem to support the viewpoint of the author. Some subjects are presented in such detail that in a book of its size other perhaps equally important material must be slighted.

On some matters the author is quite opinionated: i.e. the use of BCG vaccine. In his zeal to dispose of this subject he neglects to give any consideration to some seemingly reliable reports from many different investigators. Dr Myers does however show dramatically what can be done in tuberculosis control without use of attempts at immunization. His documentation of tuberculosis control methods in Minnesota is fascinating and the excellent results of the program attest the significance of his contentions. The sections on control methods, the use of the tuberculin test, and his offensive attack on the tubercle bacillus are well worth reading. Those concerning the clinical aspects and treatment of the disease are sketchy at best with undue emphasis

on certain subjects while neglecting more important ones. The book presents background material on the subject of tuberculosis which may well be read with profit by anyone interested in tuberculosis but I cannot recommend it for a guide to diagnosis or treatment.

—JAMES A. WIER Col MC USA

**THE MERCK VETERINARY MANUAL** A Reference Handbook of Diagnosis and Therapy for the Veterinarian 1385 pages thumb-indexed Merck & Co Inc Rahway N J 1955 Price \$7.50

This first edition is an excellent reference handbook of diagnosis and therapy for the veterinarian as well as others interested in diseases of animals. It is patterned after the *Merck Manual of Diagnosis and Therapy* and incorporates the advances in form and style made by that publication since 1899. Some 200 contributors cooperated in its preparation. The arrangement of the contents in parts and sections with a list of chapter titles and subtitles at the beginning of each section, the complete index with cross listings, and the alphabetical thumb index make it a convenient and timesaving reference. The basic parts of the book present the following broad topics: Diseases of large and small animals including nutrition, toxicology including herbicides, insecticides, bacterial toxins, and chemical poisons; diseases of poultry; health and disease problems of animals maintained in laboratories, on fur farms, and in zoos; and an addendum with public health and other useful ancillary information. The listing of an editorial board would give greater authority, and specifically naming contributors would add considerably to the value of the material. The reviewer believes that this publication will prove most popular and useful to the doctor of veterinary medicine as the *Merck Manual* has been to the physician. —ROBERT R. MILLER Col USAF (VC)

**THE YEAR BOOK OF PEDIATRICS** (1957-1958 Year Book Series) edited by Sydney S. Gellis M.D. 469 pages illustrated The Year Book Publishers Inc. Chicago Ill. 1957 Price \$7.50

Edited again by Dr. Sidney Gellis, the 1957-1958 Year Book of Pediatrics brings to the reader a thoughtful selection of articles appealing to the practicing pediatrician. The sections on the premature and newborn, and nutrition and metabolism are good, and statements by guest commentators round out some controversial articles.

Under infectious disease and immunity, a number of extremely interesting articles are presented. The gastrointestinal and genitourinary tracts receive excellent coverage, as well as those on the cardiovascular system and blood. With the present emphasis on screening of murmurs and congenital heart disease, pertinent articles will find more interested readers. A number of very good articles are included in the section on endocrinology, together with some good illustrations. Orthopedics receives adequate space, including discussions on steroid therapy in transient synovitis of the hip. The reader will find some absorbing articles on neuropsychiatry. Allergy

and dermatology are rather briefly presented and dentistry and otolaryngology barely mentioned

Illustrations are fairly numerous and of fair to good quality Comments by the editor are succinct and interesting Discussions by a few of the guests are at times verbose and take up space perhaps better devoted to additional articles Emphasis continues to be given to articles of immediate use and current interest A very worthwhile book —MILTON KURZROK, Capt MC USN

THE LOWER URINARY TRACT IN CHILDHOOD S m C rrel d Cl l  
d R tg l g Ob rv t by S R l d K j llb g N l  
Ol / E c d Ulj Rudb 298 p g ill trat d Th Y B k  
P bl h I Ch c g Ill 1957 P i \$18

The authors have presented in an excellent manner the variations of normal and the abnormalities of the lower urinary tract in children The subject material consists of children age 1 day to 15 years totaling 1461 cases seen or treated by them

The text begins with separate chapters on embryology anatomy and physiology which are beautifully portrayed with excellent illustrations and reproductions of x rays These sections are very complete and easily understood which in itself makes the book worthwhile Subsequent chapters consider each abnormal entity encountered in childhood separately again with many fine reproductions of urethrograms and cystograms which are correlated with the text Most of the abnormalities described are congenital in origin as expected and under each heading the authors present their treatment and results of such treatment Many cases are presented with excellent x rays showing the findings initially during treatment and after treatment The only topics not discussed in this book are hypospadias epispadias and and exstrophy of the bladder which were treated by the plastic surgery units in Stockholm

I believe this book is an excellent addition to the growing list of texts on urology It should be read and studied by all urologists pediatricians and general surgeons who see some of these unfortunate children usually when irreversible damage to the urinary tract has already occurred An excellent reference table at the end of the text book should be invaluable for any one wishing to study separate topics in more detail —NICHOLAS MALLIS Maj MC USA

DIGITALIS C mp l d and ed t d by E G y D m d M D 255 p g illu-  
t t d Charl C Th m P bl h Sp ingf ld Ill 1957 P \$7

This monograph is an outgrowth of a two-day postgraduate program on digitalis given in February 1956 at the University of Kansas Medical School The material presented by representative investigators provides fairly complete coverage of the digitalis glycosides encompassing their history pharmacology physiology experimental approaches toxicity and therapeutic use This compilation suffers somewhat from

the usual defect namely lack of editing as concerns style and ease of expression so common to books of multiple authorship. Better portions of the text are found at the beginning and the end. It begins with the classic description of digitalis by William Withering as reprinted from Major's *Classic Descriptions of Disease* and ends with a panel discussion moderated by the editor which contains much information of practical value.

In summary this book adds to the organized knowledge in cardiology. The bibliography given by each discussant is comprehensive and authoritative. Its use is recommended by internists and cardiologists. The book can well be made part of the hospital professional library.

—ARCHIE A. HOFFMAN Col USA (MC)

**THE POSTOPERATIVE CHEST: Radiographic Considerations after Thoracic Surgery** by *Hi am T. Langston M.D., Anton M. Pantone M.D. and Myron Melamed M.D.* Publication No. 11. The John Alexander Monograph Series on Various Phases of Thoracic Surgery. A Memorial to John Alexander (1891-1954) edited by *John D. Steele M.D.* 228 pages illustrated. Charles C. Thomas, Publisher, Springfield Ill. 1958. Price \$8.

This is another volume in the extremely fine John Alexander Monograph Series on various phases of thoracic surgery. This great surgeon is being honored by his students and associates with the high tribute of these monographs which will be of great interest to all of those engaged in thoracic surgery. This particular volume presents the radiographic considerations after thoracic surgery. The reproductions of the x-ray films are extraordinarily good and are accompanied with clear line drawings and a brief clinical summation with radiographic interpretation. This is an unusual book and unexcelled.

—JAMES H. FORSYTH Brig Gen. MC USA

**AN INTRODUCTION TO MEDICAL MYCOLOGY** by *George M. Lewis M.D., Mary E. Hoppe M.S., J. Walter Wilson M.D. and Oda A. Plunkett Ph.D.* 4th edition. 453 pages illustrated. The Year Book Publishers Inc. Chicago Ill. 1958. Price \$15.

This is the fourth edition of this important book. Previous editions have been the work of Lewis and Hopper; however, this one bears the names of two additional coauthors, Wilson and Plunkett. This is a practical treatise on fungus diseases and documents both clinical aspects and laboratory characteristics of the various pathogenic fungi. Common contaminants are also discussed. All material is presented in a logical, concise, clear, and readable style.

A major change has been made in the format of this edition. The clinical and laboratory phases are no longer separated but are considered together in the same chapter. Each of the pathogenic fungi is presented in this manner. In addition, the authors have taken the first steps toward replacing clinically descriptive terms by etiologic ones, believing that this is the proper approach in the description of disease processes. Illustrations are an essential and valuable part



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References to published literature should be listed at the end of the article in the numerical order in which they are cited in the author's text Care and accuracy in their preparation will expedite publication of the article Following are correct examples of references

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*Lancet* 2 621-624 Nov 11 1944  
Cabot R C Pernicious and secondary anemia chlorosis and leukemia  
In Oler W (editor) *Modern Medicine* 3d edition Lea & Febiger Philadelphia Pa 1927 Vol 5 pp 33-100

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SERVICE ARTICLES ☆ REVIEWS OF NEW BOOKS

CLINICOPATHOLOGIC CONFERENCE ☆ CASE REPORTS

VOL IX

JUNE 1958

NO 6

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UNITED STATES  
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WASHINGTON 1958

## Monthly Message

During recent months two statements have appeared in the press about Marine Private Matthew J. McKeon: one concise and dignified and the other with the same intent but with thinly veiled mockery of the commissioned officers of the Marine Corps. Both announced the fact that Pfc McKeon has been named Marine of the Month at Cherry Point, North Carolina, where he has been stationed. One article pointed out the wisdom of former Navy Secretary Charles S. Thomas in reducing the original court martial sentence. In his statement of commutation of sentence Mr. Thomas said: "I recognized that the road back would be a hard one. I am giving him his chance." Secretary Thomas performed a great humanitarian act with true insight into human character and I am sure that this has added greatly to the morale of the Marine Corps and the faith in their officers and their civilian Secretary.

The other article was most unfavorable to the junior officers of the Marine Corps. This possibly was based on the conclusions drawn from a single interview and no mention was made of the part of the Officer Corps in the planning of the entire training program together with the necessary close cooperation of junior officers and noncommissioned officers in its consummation. Furthermore, no mention was made of the fact that in time of war the junior officers as company commanders, and along with the sergeants as platoon leaders, sustain proportionately the highest mortality and wounded in action rate of any group and the same may be said for their counterparts in the Army.

To one who has intimate knowledge of the Marines in World War I, who was associated with them in the landing operations in Southern France in World War II, and who visited their front lines in Korea in the winter of 1951, it is obvious that neither the officer nor enlisted corps needs any defense but rather are to be commended for their high esprit and cooperation with and support of each other.

*Frank B. Berry*

FRANK B. BERRY, M.D.  
Assistant Secretary of Defense  
(Health and Medical)

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# Foreword

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FRANK B BERRY M D

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S g G l U t d St t N y

MAJOR GENERAL DAN C OGLE

S g G l U t d St t A F

# UNITED STATES ARMED FORCES MEDICAL JOURNAL

Volume IX

June 1958

Number 6

## ECOLOGY OF DISEASE IN WORLD HEALTH

JACQUES M. MAY, M.D.

THE concept of global epidemiology, which Dr Simmons did so much to develop and to teach, has a tremendous fascination for those physicians who consider human disease as a maladjustment of human populations to their environments rather than as an accident in somebody's life. Such a maladjustment the global epidemiologist believes can potentially be corrected by adequate cultural traits. Here we have the whole problem of world health in a nutshell: disease patterns are the expression of cultural failures. I hope to vindicate this statement as our discussion develops.

At the outset of this talk I would like to state that its purpose is to define the new concept of medical ecology and to show how its study is essential to understand the world health problem.

The student of medical ecology and disease geography, two closely related fields, is confronted with two possible approaches. He may consider political units first—unfortunately, statistics do not come by geographic regions—and explore disease occurrence in these units after or he can take one disease at a time first and build a global picture of its extension throughout the various regions of the world after.

Dr Simmons and his associates in their book *Global Epidemiology*, used the first of these two approaches, and started their presentation of disease distribution with a description of the

Annals of the New York Academy of Sciences, June 1958, Dr. May is Head, Department of Medical Geography, Anthropology, and Geographical Society, Broadway at 156th St., New York, N.Y. He is also a member of the New York University College of Medicine and a member of the Harvard University School of Public Health.



geographic layout followed by a study of disease occurrence in the area. This is a very useful and convenient approach especially for the public health researcher who knows where to look for data he needs in each country.

The second approach taking one disease at a time, and building the map of its extension throughout all the regions where it is known to occur is the approach that we have used in compiling our *Atlas of Diseases*. This method has advantages for the epidemiologist who wishes to explore the reasons for disease occurrence. Once possessed with a map of disease the study of the environmental and cultural factors that are present throughout the area of occurrence reveal the minimal requirements needed for the disease to exist.

These requirements can then be investigated on a world wide basis and a comparison of their respective importance in various places becomes possible. Both approaches of course complement each other and they are both indispensable to understand the ecology of disease.

#### DEFINITIONS

I am using the words "ecology of disease" knowing full well that they are controversial. But controversy is the basis of intellectual life and I do not feel I should make an apology for throwing around an idea because it arouses controversy.

A friend of mine, a distinguished practitioner in the city of New York, remarked to me one day, "Why do you always use this word ecology? Nobody knows what it means." More recently, my friend Gurney Clark, head of the Department of Epidemiology of Columbia University, told me that he preferred the term "natural history of disease." As Gurney knows the meaning of the word ecology, his criticism impressed me much more.

Another critic agreed that there are ecological problems involved in medicine but doubted whether one should speak of the ecology of diseases. One can conceive, he said, discussing the ecology of a living thing, a plant or a vector, but not of a phenomenon such as disease. My answer to these critics is that the word ecology means the science of the habitat of the home and that it connotes the idea of focus, of nest, as the Russian disease ecologist Pavlovsky puts it. This notion of disease having a cradle, a fatherland, a habitat whence it spreads to other areas is basic to global epidemiology which is the science that studies all the nests or foci or homes of disease and the way they reach areas of the world outside their homes. It is of value to be aware that some diseases have a focus, for example, cholera, that the conditions existing in

this focus are indispensable for the disease to occur and that outside their foci the disease does not occur unless its factors do a job of adaptation. Thus, I hold that the phrase "ecology of disease," including the idea of focus (which alternate expressions do not include), is worth retaining in our vocabulary.

In order to justify further the title of this presentation, it is needful to go back to basic definitions. What is disease? Up to very recently, the concept of disease had a very individual, very local ring. It meant symptoms and treatment. One ill, one pill, one bill. This is a legitimate approach of course, but not satisfactory to the public health worker, nor to those who follow Dr. Simmons' teachings, think in a global way, and want to learn more about more, rather than more about less. To the disease ecologist, *disease is that alteration of living tissues that jeopardizes the survival of the individual or of the group in the environment in which it occurs*.

This definition has the advantage of introducing the all important notion of environment. Indeed, normalcy cannot be defined per se. Disease is a relative thing. Further, the same tissue change does not constitute disease everywhere.

Recently, Sir George Pickering, the Professor of Internal Medicine at Oxford, England, took me to task at a meeting, where we were seated together, because I had suggested this definition which he said did not help the practitioner in his daily problems. A few moments later Sir George was trying to define the boundaries between pathologic and physiologic high blood pressure—what is a normal blood pressure? What could be a criterium for hypertension? Of course, there cannot be an acceptable definition of the normal, so I suggested to him that hypertension becomes pathologic when it jeopardizes the survival of the patient, either on a short-term, or on a long-term basis in the place where it occurred. Being a good sportsman, he had to agree.

The same tissue alteration does not constitute disease everywhere. The Indian living at an altitude above 10,000 feet in the Andes has 8,000,000 red blood cells per cubic millimeter, as well as a higher degree of blood viscosity, a larger heart, and, in general, a lower systolic blood pressure than the man living at sea level. He most probably also has other, as yet not explored biochemical traits which might be considered pathologic should they occur in a different environment. Perhaps we also can add boldly that the group of people possessing the S type of hemoglobin in a malarious environment are not as sick, if they are sick at all, as the same group would be in a non-malarious environment.

## HOW DISEASE OCCURS

Disease must be understood on an area basis. If disease is recognized to be that alteration of tissues placing persons in jeopardy which we have just said it was, what are the factors needed to bring about such an alteration?

For the convenience of the discussion we can group under three headings the factors playing a decisive role at a certain place and at a certain time in the occurrence of disease or in the formation of a disease pattern. First we must have a stimulus from the environment. Second we must have a response from the host loud enough to be detected, if not by clinical exploration at least by using the modern instruments of modern medical technology. The degree of this response of course depends upon the amount of stimulus applied in relation to the genetic make up of the host. Third the disease pattern is governed by the operation between stimuli and host of this edifice of customs, habits, and techniques that we call culture.

These traits either bring stimulus and host together, thus creating the chance for disease occurrence or keep them separate thus preventing the disease. When this happens there is at the place considered a disease potential that is replaced by actual disease if and when the cultural trait separating stimulus and host breaks down or disappears. It is on this three cornered basis—stimulus, host, and culture—that the science of the ecology of disease is established. It is the study of these disease factors, their geography, their mapping that gives us our understanding of disease occurrence on an area basis and forms the structure of a global epidemiology.

## ENVIRONMENTAL STIMULI

**Physical Stimuli** First among them are the so called physical stimuli those that geographers include in their definition of climate. Few physicians realize that we know extremely little about the influence of these physical climatic factors on man as a host. Dr. Douglas K. Lee, formerly of Johns Hopkins and now with the Quartermaster General, established an interesting diagram based on the combined plotting of temperatures in abscissas and humidity expressed in vapor pressure in ordinates. Within this area Lee defines several zones: a zone of comfort below or beyond which nobody is comfortable; a zone where muscular performance begins to deteriorate; a zone where mental performance deteriorates; and a zone of distress. It is possible to superimpose on this chart another chart based on the range of mean monthly temperatures and humidity for sample locations. Thus it can be seen how the people of Rio de Janeiro or Basra fare in comfort or discomfort and under which limits

exertions can be expected from them. Beyond this knowledge, loosely measured by the terms comfort and distress, our gaps of knowledge on the effects of climate on man reach the proportions of an abyss.

The reasons for our ignorance on matters of climatic influence on men is that it is impossible to separate in nature the physical elements of climate from the living things that have established their habitat in these climates. When our grandfathers used to speak of good or bad climates they meant climates where no outside aggression attacked the body, or climates where such aggressions occurred. What they considered to be climate, essentially, meant the disease agents that unknown to them existed in these climates. When climates are reproduced in artificial chambers, the result is a distorted picture, because many unknown elements existing in the outside world, such as heat and humidity, are not present among the variables.

We are just beginning to realize the existence and possible importance of such unknown variables as cosmic rays, static electricity, radiations, and probably still other material forces that have no name. If it is possible that flares in the sun may disrupt what I might call "macroscopic" electronic communications on earth, then it is likely that they also may produce changes in the "microscopic" electronic communications that occur in things around us and in ourselves, and probably are intimately involved in the make up of what we call life.

The forces of climate conceivably may influence our resilience to disease in an indirect way, the same as they do in the chicken. We all remember Pasteur's<sup>2</sup> experiment with anthrax which he was unable to induce in his chickens until he lowered their body temperature by plunging them in an icy bath, after which the inoculation was successful. The condition of stress, as we called it for lack of a better understanding of what happened, created in the chicken a susceptibility of disease that had not existed before.

Further, the physical elements of climate, those we know how to measure and those we don't influence the things we eat and the agents, vectors, intermediate hosts, and reservoirs that bring us our transmissible diseases. The whole field of climatically induced mutations in agents, vectors, and hosts is practically unexplored.

To a large degree, these physical elements of climate also govern men's cultures from the material that is made available to build human dwellings to types of architectures, diets, and means of transportation. The air, the water, the earth, and the temperature, govern what happens to places, as good old Hippocrates could have said and thus govern the disease pat-

terms So far we physicians have done little to explore the fields of geology geography climatology meteorology and physics with the purpose of relating the findings of these sciences with disease occurrence My humble contention is that more teamwork between disciplines is needed along that line and would repay a large amount of dividends in knowledge

**Biological Stimuli** The second group of stimuli challenging human survival comprises all the living things who have elected to inhabit the various niches as ecologists say the macro and the micro climates An important aspect of the coexistence agreements developed by these living things which the physician and even the public health worker often forgets is that these living things like men live in societies Here I have to bring you a definition of what the medical ecologist understands by the word society *A society is a pattern of mutual tolerance that occurs temporarily among living things when the dynamism of reciprocal exclusion has been exhausted*

The idea in these condensed words is to stress that a social structure is essentially temporary based on mutual tolerance A mutual tolerance implies dominance and submission and the moment anything happens to disturb the equilibrium of this pyramid of this compromise the pattern is upset new dominants come to the top with unpredictable results The reason for all this of course being that whatever size they are infinitely small or tremendously big living things always compete for food and shelter

I believe that it is profitable for the medical ecologist studying the occurrence of transmissible diseases throughout the world to remember that in all likelihood bacteria—and who knows perhaps also viruses—snails mosquitoes rodents and mammals all live in society It is on this concept that the modern therapy by antibiotics and in many instances disease control is based Indeed in a room loaded with an aerosol of *Penicillium notatum* the transmission of pneumonia among human hosts would not occur for lack of a live pneumococcus in a paddy field sown with gambusia *Anopheles jeyporiensis candiensiensis* would have a tough time really surviving and so would *Plasmodium vivax* for lack of adult mosquito habitat in which to spend its sexual life

It has been shown that it was difficult to have yellow fever virus multiply in an *Aedes aegypti* previously fed on dengue virus Could it be that these two viruses do not belong to the same social structure in spite or because of their relationship? The social structures of living things are closely de-

pendent upon the geographic factors and the food availability discussed above, which is why we find these societies closely integrated and almost identified with the various geographic areas in which they occur

### RESPONSES FROM THE HOST

I particularly wish to discuss now the global epidemiologist's approach to the study of this response from the host. There is very little known on this subject, we have paid scant attention in the past to this host. Our textbooks and our literature are full of studies on the living stimuli but offer very few on the host's structure, on the genetic make-up of the man who presents the symptoms, and on the relationship between genetics and biology.

We have, so far, not been able to manage any classification of hosts on the basis of their response to environmental stimuli. We have no map of susceptibilities and immunities. The psychiatrists are the worst offenders along those lines. They have concentrated so much on the study of the stimuli, conscious and unconscious, that they have almost completely forgotten the patients, and they speak of functional versus organic disorders as if anything functional could occur in a vacuum and could be understood without an exhaustive study of the physical structure supporting it. I believe that the medical ecologist can make an important contribution to the understanding of disease, any disease, by showing that as much attention must be given to the study of the host as is given to the study of the stimulus.

What lies at the basis of the response any individual or any group offers to environmental challenges? Obviously, the genetic make up. We all know that the genetic make up of an individual is represented by the sum total of his genes (his genotype) and by the appearance of his genotype at a given time (his phenotype).

If it is true that the concept of "one gene—one enzyme" has value, then we can understand why certain people or animals are susceptible to certain diseases and others are not. Why is leprosy essentially a human disease and why is foot and mouth disease essentially a cattle disease? Why do cholera vibrios multiply in the intestines of guinea pigs without causing them any harm? Why can't birds catch human malaria? The enzymes governing these agent-host relationships are there or not, the genes that support them are present or not.

All these problems underline the considerable importance of the terrain. We recently have been given interesting hints along these lines. Some studies seem to indicate that individuals

belonging to blood group "O" are particularly susceptible to the stimuli that result in the development of peptic ulcers.<sup>4</sup> The role of the so called hemoglobinoses in shaping the responses to pathogenic stimuli is certainly worth exploring thoroughly. We don't discuss any more the fact that the sickle cell trait protects against *Plasmodium falciparum*.<sup>5</sup> We have reached the stage where we seek to understand how. It would be of great interest to find whether hosts having the Kell system or any other system in their blood and who belong to this or that blood group are not more susceptible to this or that disease than hosts with another genetic make up. All this seems to outline an important field of investigation for the future.

The genetic establishment of an individual or of a population is more closely linked with the environment than we currently realize. The genotype of a population is what it is and becomes what it shall because of the presence of environmental stimuli and pressures that cause *mutations* and force living things into *migrations*. Mutagenic factors are little known; however heat, chemicals, radiations and probably others are specific to their environmental niches. The way they combine gives the macro or micro climates in which things live their characteristics. These climates exert their influence on the genes of vegetables and animals alike, causing mutations that upset the social patterns referred to above, causing dominants to lose their dominance and submissive elements to acquire dominance.

When we say this year was a bad year for cholera, there was too much heat and humidity, we may be giving only a partial description of what occurred, because it could very well be that the cholera vibrios living in that area have mutated from a mild strain into a virulent one through the effects of heat, humidity or radiations. This of course can also be true of the influenza virus and of any other agent, vector or reservoir we can think of.

When the environment exerts its pressure and when this pressure gets to be too painful for any living group to accept, the group usually flees that environment. This occurs when animals migrate and when European populations come to America to escape political pressures in the old continent. The result of these migrations at every level, from disease agents to man, are to mix up genes and to create a new genotype in the particular environment to which these biotic refugees have fled. Thus it is justified from the genetic angle as well as from all others, to link the disease pattern with geographic pressures.

As for the phenotype, its relation to the pressures of the environment are only too obvious. Genetic material is like a pellet of clay of a certain weight, mass and density. This we

can shape into the figure of a woman, a horse, or anything else. It is still the same pellet of clay with the same weight, the same chemical structure, the same genotype; however, under the pressure of the environment (in this case, the fingers of the artist) the phenotype looks like a woman or like a horse.

In the same way, the environment in which man lives, pressing his genotype, brings about new shapes, new phenotypes that may be useful for continuation of living in that same place, or that can be detrimental. If a man has lived for a certain time in a certain environment, he has been bitten and hurt, and has suffered emotions that are specific to the place. All these stimuli have left scars, the sum of which form his personality and govern his future response to further stimuli. Some of these scars are beneficial (immunities and education), some are detrimental (allergies and neuroses), and it is the total of these scars that governs the disease pattern by governing responses to the stimuli present in the environment.

### CULTURAL FACTORS

The third group of forces that intervenes in the disease pattern is the culture of the various human groups that grow in the infinite variety of physical and biological environments. Here we come to the definition of a word that the medical ecologist has to use repeatedly: this word is "culture." *To the global epidemiologist, culture is the sum total of the concepts and techniques that individuals or populations use in order to survive in a given environment.*

That, of course, does not mean that all cultural traits are survival worthy, if I may be forgiven for the use of a barbarous word. It is quite possible that many cultural traits will lead the group to its destruction rather than to its survival. A case probably could be made to show that originally these traits have developed because they were mistakenly thought to promote survival or because they did promote survival at the time when they were adopted, but have ceased to do so when circumstances changed. People do not give up their culture easily; they like to feel the protection of their ancestors around them, and they would rather die doing something that has always been done than survive by not doing it, or trying something that has not been tried before.

The origin of culture is truly the job of anthropologists, and I am not competent to discuss it. My point of view is that of the epidemiologist: we ecologists of disease are only interested in finding out whether a cultural trait promotes disease or prevents it. My definition of culture has no other object than to help decide when we are confronted with a cultural trait and whether it is helpful or detrimental.



For instance in Southeast Asia we deal with a population whose culture implies walking barefoot on a heavily polluted soil. We can say that this is detrimental—yet in certain villages of India, the villagers place wooden boards on the soil of the defecation areas. This reduces the contact between feet and polluted soil and prevents to a certain degree the mixture of earth and fecal matter that is needed for the hookworm larvae to develop. As a result in such villages the hookworm rate is much lower than where the defecation area is not protected by such boards.

A similar favorable effect on hookworm disease obtains in China in the areas where the silkworm industry rather than rice cultivation flourishes. In these areas the farmers spend much time on ladders tending the mulberry trees and have much lower rates of hookworm infection than the rice growers.

Yet culture carries its many threats to survival often such threats are a counterpart of developments intended to prolong survival. Such are the many examples of man made malaria and in our own culture the possible role in producing disease patterns of insecticides that seep into the soil and may be recovered in the crops of butter coloring with its possible carcinogenetic nucleus of food preservers and even just plain excessive eating of fat-producing molecules which we are persuaded to do by the loudly advertised requirements of our ever growing industry. Cultural traits also influence disease patterns in many indirect ways. The physical environment not only shapes societies of living things as we have seen but it also shapes cultural patterns and hence the diseases that arise within these patterns.

The example of the farmers in northern Vietnam is interesting. These people live in one of the two or three most densely crowded areas of the world. The density of population is around 900 per square mile. The houses and the villages they form represent from the point of view of the way they are built a compromise between the material that is available and the need to save as much soil as is possible for food crops. The material available is mud and rice straw which does not lend itself to sky scraping architecture. Thus there are very few two-story houses in the villages of the Red River Delta. The dwelling place usually consists of a mud bungalow with the pigsty on one side and the kitchen on the other. Please note that there are no fierce malaria vectors in the area.

Some sixty miles to the north in the hills we find a different cultural trait also very much influenced by the physical environment. In the hills lumber is abundant but there is little rice straw and little mud. The people for reasons that are not

fully understood, build their houses on wooden piles, which places what we would call their living room at an elevation of 12, 15, or sometimes 20 feet above the ground

In these hills, *Anopheles minimus*, a very fierce malaria vector, abounds, its breeding enhanced by the network of hill streams. However, it so happens that *Anopheles minimus* does not fly much higher than 10 feet above the ground. As a result, although it is essentially a man-biting insect when it has a chance, it feeds on the cattle herded under the house between the piles, because that is what it finds at its normal flight altitude. Furthermore, the cooking takes place in the house, not outside as in the delta, this fills the living room with smoke that chases away any stray vector.

Due to the congestion in the delta, several schemes have been carried out at different times in history to try to relocate delta people in the hills. These people carried their culture to the new location and started to live at ground level, to cook outside the house, and to shelter their pigs away from their dwelling. The results have been disastrous. Malaria epidemics decimated the newcomers, and the reputation of the hilly region among the lowland dwellers is that it is full of evil spirits and that no man of the delta should ever go to the hills.

When we started this discussion, we said that disease occurred when three orders of factors converged, or were present at a certain place, and at a certain time: stimuli from the environment, cultural factors, and a response from the host.

### THE ECOLOGY OF DISEASE

The ecology of disease governs our understanding of world health because it is based on the study of the three main chapters we have outlined in this discussion: (1) geographic study and mapping of pathogenic stimuli and factors of disease, (2) geographic study and mapping of the genetic characteristics of the host, taking notice of the known immunities, susceptibilities, and biochemical and physiological traits; and (3) geographic study of cultural traits linking together or separating stimulus and host.

Many concrete examples of what is stated above could be given. It is obvious that it applies to transmissible diseases but it also applies to noncommunicable diseases. The problem of world hunger is a good example. It is fairly easy to discover where people are starving or suffering from malnutrition. We know how important this problem is in our days, and our country has not turned its back to it, but it is not sufficient to know

that two thirds of the world's population does not eat to its satisfaction nor is it sufficient to know where these starving people can be found. What we want is to find out why they are starving and what are the circumstances of human ecology that in each place create the want. If we do not know the constitution of these different pictures throughout the world our help will be ineffective and wasted.

In some countries malnutrition is the result of scarcity there is not enough food for the number of people to be fed or the food is of poor quality short of the molecules the tissues of the host need and want. In other countries the problem is cultural. In certain parts of India and Southeast Asia the social structure of the society is a serious cause of food shortage the customs governing inheritance divide and subdivide the land to such a point that it is not soundly workable.

In Mexico in certain parts of Africa in the Caribbean Islands and again in India there is a competition between men and animals for the food that can be produced so both starve. In other places food resources are not used as they should be for instance in the Lake Chad region cattle are currency a sign of wealth a local means of exchange. Eating a cow would be like eating one's capital. Little is done to increase milk supply. The food possibilities are not exploited as they should be.

In Brazil the transportation facilities are inadequate food cannot be brought from one province to another when needed. In Colombia except for the Magdalena Valley area a peculiar setup leads to semistarvation. Much land is used as a security against inflation not as a good producer. Good land is used for cattle grazing on an inefficient basis while most food crops are grown on small farms often on steep slopes and in poor soil.

Elsewhere we find that cultural taboos play a role. People starve in Bengal rather than kill a cow or even eat the flesh of one that has died. In some other places especially in South America and in North Africa hunger is fostered by absentee ownership of large estates where tenants raise cash crops instead of food. In some places again as in India and China you find combined together population pressures exhaustion of arable land poor farming techniques cultural taboos, poverty social and economic restricting cultures and lack of capital.

The occurrence of deficiency syndromes also may be influenced by the genetic make up of the host. There is some evidence that certain Polynesian groups thrive on diets that would

be unsatisfactory to Crucasians \* Do their genes provide them with the power to synthesize amino acids which the Crucasians have to find ready made in their diets?

### THE CHANGING MAP OF DISEASES

I should like to add a word about the changing map of disease and the changing maps of disease factors. These maps have to change. First, because the environment changes: as alluviums fill up estuaries, isolated villages are replaced by large cities. The diseases that were prevalent among the sparse population of Manhattan when Captain Hudson came sailing to our shores, are not the same as those that prevail today at the same place. When jungles are cleared, as in parts of Malaya, or are allowed to reconquer the land as on the site of the dead city of Angkor, new societies of agents, vectors, and hosts nestle themselves in the new niches. Each culture brings about its set of diseases.

It would be of great interest, if data were available to write a study of the disease patterns that have accompanied cultures that have run their course and are no more. Whenever possible, history of medicine should focus on the relationship between disease patterns, as far as they can be ascertained, and the climatic, biologic, and cultural niches in which they were established. Example: We have just begun to open the chapter on the diseases of radiation.

The map of diseases also changes because of migrations. It is one of my cherished projects to compile a map and to write the attendant discussion on bird migrations. I imagine that such a project would be of interest to virologists.

In conclusion let me tell you about a cartoon I saw a short while ago. I am sure Dr. Simmons would have liked it because of its implications. It represents an old Chinese couple in some remote village of China. The man is blowing his nose, and the woman says: "Little did you know when you started those few sneezes some months ago that you would become a world figure." Eleven years ago another man became a world figure, his name was Mr. Lebar. We should remember Mr. Lebar because General Simmons introduced his book on Public Health in the World Today by reminding us of the international bus ride that this gentleman took to return to New York from Mexico in 1947. By doing so Mr. Lebar started a smallpox epidemic that resulted in a huge vaccination campaign in the United States, costing millions of dollars.

Thus at all times the health of tomorrow is prepared and hatched in the remotest corners of the world. We should try to

keep informed in regard to these events. We should try to recognize the birth of new stimuli to disease, the changes that occur among the social structures of agents and vectors, and the changes in the maps of immunities and susceptibilities. We must keep abreast of the cultural changes that either create new links between agents and hosts or erect protective shields between them. This we must do if we are to follow the great lines of Dr. Simmons' global thinking, and if we are to live up to the expectations of the world that our country will be a leader in the field of world health.

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# ALKYLATING AGENTS A BRIEF REVIEW

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CHEMOTHERAPY of the leukemias and related diseases has advanced considerably since 1942, when in the midst of World War II Goodman and Gilman,<sup>1</sup> then at Yale, discovered that nitrogen mustard could substantially reduce the tumors of lymphosarcoma and Hodgkin's disease. For the next few years research into the effects of such agents was classified, and only a few observers<sup>2</sup> made the primary observations that led to the general use of nitrogen mustard in Hodgkin's disease and lymphosarcoma. In recent years, many new "alkylating" agents have been developed, chiefly by Haddow and his colleagues at Chester Beatty Institute in London. A recent symposium of the New York Academy of Sciences<sup>3</sup> was devoted to the alkylating agents, and marked the 15th anniversary of the introduction of nitrogen mustard. The symposium, attended as it was by over 600 observers, may be said to have been a monument in honor of the Chester Beatty group, which has done so much in recent years to develop new agents, some of them, like Myleran (brand of busulfan), having possible selective activity.

Discovered by Ritchie in 1854, mustard gas and related compounds were regarded solely as toxic agents suitable for chemical warfare, and their effectiveness was well documented during World War I.<sup>4-6</sup> During World War II there was another demonstration of the effects of these agents, this time quite by accident. The Port Bari incident,<sup>7</sup> in 1943, showed dramatically and tragically the effect of mustard-like agents on humans. At that time the Allies had invaded southern Italy from North Africa, and an important seaport in the chain of supplies was Port Bari, Italy. In the interest of preparedness a ship was anchored in the harbor containing a cargo of 100 tons of mustard gas, in addition to explosives. On the night of 2 December 1943, a German air raid was particularly effective, sinking sixteen ships and partially destroying four others. The ship containing the mustard gas and explosives was hit directly with loss of all crew members, and the mustard was spread over the harbor,

F m b Bl d R arch L bor tory W l m D m hek M D Direct r and  
Z kind R h L b rat r N w E gl nd Ce t r H sp tal Boston, M s Comdr  
M F r l d now ign d t U S N I H sp tal B th da, Md.

where it mixed with and dissolved in a layer of oil. Those rescued from the water had suffered prolonged exposure to the resulting mustard in oil. To make matters worse because there was no one alive with knowledge of the presence of mustard this fact was not recognized in the confusion and many of the rescued were allowed to remain in their oil soaked clothes for 12 to 24 hours. As a result there were 617 hospitalized casualties from mustard exposure of whom 83 died. Deaths occurred mainly on the third day from acute systemic effects of burns and on the ninth day as the result of pulmonary infections with leukopenia. Of particular interest were autopsy reports describing shrunken spleens with wrinkled capsules. In the few cases where marrow examinations were done the marrow was described as pale pink and dry.

Aside from this dramatic accidental demonstration of the effects of mustard like compounds research work was conducted by selected small groups as a result of the therapeutic demonstration by Goodman and Gilman. Consistent with wartime security measures the various mustard compounds were given code letters as follows:

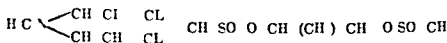
HN	—	bis (B chloroethyl) sulfide
HN <sub>1</sub>	—	ethyl bis (B chloroethyl) amine
HN	—	methyl bis (B chloroethyl) amine
HN	—	tris (B chloroethyl) amine
TL301	—	isopropyl bis (B chloroethyl) amine

The designation of nitrogen mustard as HN has continued to the present as an abbreviation with understandable confusion on the part of those not familiar with its origin.

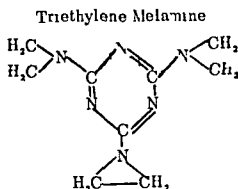
As for the term "alkylating agents" which serves as an all inclusive term for the various mustard like compounds this too may require explanation. According to basic organic chemistry<sup>1</sup> one example of an alkyl group is an ordinary alcohol minus the OH group. In the case of methyl alcohol the alkyl group would then be CH<sub>3</sub> and in the case of ethyl alcohol the alkyl group would be CH<sub>3</sub>CH<sub>2</sub> and so on. These groups do not exist as separate molecules but it is convenient to speak of them as alkyl groups and to refer to their combination with other substances as alkylation. The mustard compounds merely contain more complex alkyl groups than the alcohols described e g the formulas for nitrogen mustard and Myleran.

Nitrogen mustard

Myleran



The vertical dotted lines show where the compounds react under physiologic conditions to yield alkyl groups capable of biologic activity. Accordingly, the various agents are classified as mono, bi, or polyfunctional, depending on the number of reactive groups available. Triethylene Melamine (TEM) is an example of a polyfunctional compound with the capability of reactive alkyl groups in the three ethylene groups.



The site and mechanism of action of alkylating agents have been the subject of a great deal of investigation. The group working at the Chester Beatty Institute has done much to clarify these matters. According to their observations,<sup>1</sup> the reactive centers of alkylating agents behave as positively charged carbonium ions which have a particular affinity for electron rich groups in biological systems, such as organic and inorganic anions, amino groups, and sulfhydryl groups. The most important and most common of these reactions appears to involve the primary phosphate groups in deoxyribonucleic acid (DNA). When such a reaction is the result of a polyfunctional agent, cross linkage occurs with marked disruption of the normally straight chain polymers. In other words, the molecule of the alkylating agent with its two or three reactive centers forms an abnormal bridge between different polymers of DNA and even in the same polymer. Such chemical changes occurring in chromosomal material would be expected to produce profound effects on the process of cell division, and this is actually the case.

The reactivity time of alkylating agents appears to be very short, probably within two or three minutes after instillation in a biological system.<sup>2</sup> Excretion studies by Smith and associates<sup>3</sup> at George Washington University, utilizing radioactive tracer techniques indicate that the majority of labeled material is recovered in the urine within 24 hours as a variety of substances none of which is the unchanged alkylating agent.

Alkylating agents have been termed "radiomimetic" because so many of their effects resemble those produced by x rays.



Each is capable of suppressing mitosis and producing chromosomal injury. Therefore each of these agents is capable of producing mutations, some potentially dangerous. Myleran has been shown to produce cataracts in rats —another late complication of radiation (table 1). Of occasional importance clinically may be the fact that alkylating agents are dependent on transportation to the site of activity via the blood, whereas x-ray radiation is not. In other words, a large tumor mass with defective blood supply may respond better to local radiation whereas widespread involvement may be treated more effectively with an alkylating agent.

TABLE 1 Comparison of effects of radiation and alkylating agents

	Radiation	Alkylating agents
Suppression of mitosis	+	+
Chromosomal injury	+	+
Mutagenesis		+
Cataracts	+	+
Chromatid fusions	+	+
Stimulation of diploid tumor formation		+
Antibody formation by AET and malar compound	+	+

Amchlor ethyl carbimide-hydrobromide

Hematologic effects of alkylating agents have been studied extensively by Elson of the Chester Beatty Institute. According to his observations,<sup>1</sup> no single agent is completely radiomimetic. For example, C B 1348 Leukeran (brand of chlorambucil) has an effect on lymphoid tissue similar to radiation, whereas Myleran's effect is radiomimetic with regard to the granulocytic elements. The simultaneous administration of both agents produces a hematologic effect quite similar to radiation.

From a host of alkylating agents that have been produced and studied, five or six have emerged as effective and useful agents clinically. These are nitrogen mustard, methyl bis (2-chloroethyl) amine, Myleran, 1,4-dimethylsulfonyloxybutane, Triethylene Melamine, C B 1348 (Leukeran), p (D) 2-chloroethyl amino-phenylbutyric acid, possibly TEPA, triethylenephosphoramide, and Thio-TEPA, triethylenethiophosphoramide. In general, the effect of each of these compounds is similar in that they react with actively dividing cells, whether in neoplastic tissue, bone marrow, gastrointestinal mucosa, or elsewhere. Yet there appear to be sufficient differences in selectivity of action to render a particular agent the drug of choice for a particular neoplasm.

Nitrogen mustard has been the most available and therefore the most thoroughly tested alkylating agent, and it is still one of the most useful.<sup>12, 13</sup> It usually is the chemotherapeutic agent of choice in Hodgkin's disease and lymphosarcoma and is used frequently in carcinomas of the lung, ovary, and breast. It ordinarily is administered intravenously in a total dose per course of 0.4 mg/kg which may be given at once or in divided doses. It also may be administered intrapleurally or intraperitoneally.

Myleran has become the chemotherapeutic agent of choice in chronic granulocytic leukemia. In this disease its action has been almost completely predictable, allowing for titration of dosage according to the response in the white blood cell count.<sup>14</sup> It may be administered in doses of 4.0 to 12.0 mg daily, initially, and then reduced gradually as the white cell count returns toward normal.

TEM and C B 1348 (Leukeran) appear to be more specific against neoplasms involving lymphoid tissue; therefore, they have been used most frequently in chronic lymphocytic leukemia, lymphosarcoma, and Hodgkin's disease.<sup>15, 16</sup> Both are administered orally, TEM in a dose of 2.5 mg one to three times weekly, and C B 1348 in doses of 2.0 to 30.0 mg daily. Because TEM often is unpredictable in its depressant effect on the marrow, its use is being supplanted by C B 1348 in most cases where an oral preparation effective against lymphoid neoplasm is indicated.

TEPA and Thio TEPA have been used in a variety of malignant neoplasms with variable temporary response, but the most beneficial effect has been in ovarian and breast neoplasms where survival time may be prolonged significantly. The average dose per course of treatment varies widely (20 to 600 mg), depending on whether the agents are administered by oral, intratumor, intrapleural, or intraperitoneal routes (table 2).

That alkylating agents are capable of temporary inhibition of malignant neoplasm, there can be no doubt. But why must their inhibition be partial and temporary? There may be some acquired resistance by persisting neoplastic cells, or the answer may lie in the fact that the action of these agents is not sufficiently selective for neoplastic growth. The concentration of alkylating agent in neoplastic cells that are growing in an exponential fashion is not much greater than its concentration in the bone marrow or gastrointestinal tract, where cells are growing in a "steady state." The result may be that the cells which are growing exponentially are depressed only partially and temporarily, whereas the normally proliferating cells are sufficiently affected to preclude further therapy. The question therefore arises as to

TABLE 2 Alkylating agent / b according to usual order / preference

D	Ag				
	Myl m	N tr g m ard	TEM	L k ra	TEPA Th o-TEPA
Chro gr ul cyt l ukemi	1				
Chro lymph cyt cl ukem			2	1	
H dgk da		1	3	2	
Lymph m		1	3	2	
Ad d ar m f					
l g		1			
ary		2			1
b		2			1
My fung id		1	2		

T hyl M l m  
Triethyl eph ph m d  
Tri thyl thu ph ph m d

whether we have exhausted the possibilities of alkylating agents as cancer chemotherapeutic compounds. This may be the case but the fact remains that the alkylating agents are capable of producing profound alterations in cell growth and investigations continue in an effort to render them more selective in action by modifications in structure and combinations with other compounds.

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### LABELING OF HAZARDOUS CHEMICALS

A substantial number of packaged chemicals are not now required by law to identify hazardous ingredients on their labels or to warn users of the dangers of overuse or misuse. A recent survey revealed the sketchy nonuniform and generally inadequate pattern of regulations at the state and national levels for informative labeling of chemical products. The survey disclosed that at the national level label laws exist for drugs pesticides certain caustic and corrosive substances and narcotics. There are no federal laws for the precautionary labeling of industrial chemicals household chemicals or poisons although regulations for the packaging and labeling of dangerous chemicals and explosives in transit by land or water or via the mails are issued by the Interstate Commerce Commission and the Post Office Department.

—BERNARD E. CONLEY, Ph.D.  
in *Journal of the American Medical Association*  
p. 2154 Apr. 26 1958

# ASIAN INFLUENZA AT FORT BELVOIR, VA

## Epidemiology and Vaccination

JEROME H GREENBERG *C pt 1 MC USA*

**D**URING 1957 Asian influenza appeared at most U S Army installations in the United States. The infection first appeared in epidemic form at Fort Ord Calif during July and shortly thereafter at Fort Lewis Wash. It next appeared at Fort Carson Colo in September. At that time it was believed that epidemic influenza would appear shortly thereafter in installations in the eastern United States and it was decided to study the disease at a representative training post convenient to this institute.

Fort Belvoir Va in addition to satisfying the above requirements provided a training program in which there was a rapid turnover of students from all parts of the country. It was thought that Fort Belvoir would undoubtedly experience an epidemic of Asian influenza. It therefore was decided to set up a study that would describe such an epidemic, relate complications to bacterial flora and evaluate the effectiveness of the influenza vaccination program on post. This report will be limited to describing the epidemic and the vaccine evaluation.

### THE POST

Fort Belvoir Va is a major U S Army military installation located about 15 miles south of Washington D C on U S Route 1. The major function of the post is the training of personnel for the Corps of Engineers. All personnel have had some previous military training and therefore are not classified as recruits.

Approximately 30 per cent of the post military population are students in advanced training courses lasting from 2 to 16 weeks. These students have already received basic training and the majority leave Fort Belvoir upon completion of their training. The rest of the post military population are "permanent party" personnel who perform the routine administrative and maintenance operations, participate in the management and training of the students and engage in other military activities. Permanent party personnel generally remain at Fort Belvoir for much longer periods than do the students.

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weekly acute respiratory disease incidence rates for all units could be calculated

The course of the epidemic is shown in figure 1. The sudden sharp rise which occurred on Monday 7 October reached a peak on 9 October then dropped to pre epidemic levels on the weekend. A similar picture was seen in each of the two following weeks although at progressively lower levels. The peak attained in the fourth week was within the usual seasonal range.

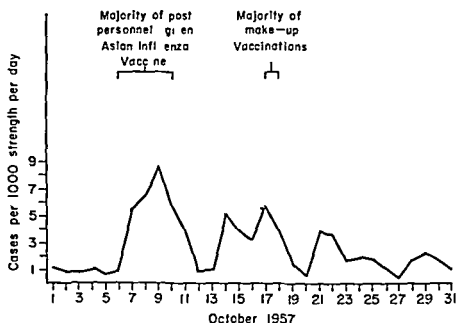


Fig. 1. Acute respiratory diseases at Fort Bliss, Va., October 1957

Table 1 shows the incidence in 19 units of acute respiratory disease necessitating more than a 24 hour absence from duty during the epidemic period. Those units marked USAECP (U S Army Engineer Center Regiment) and the USMA Prep School are student groups; the rest permanent party units. The student units contained approximately 5 per cent nonstudent administrative and supervisory personnel.

Of the 19 units listed, 15 attained their peak incidence in the initial period of the epidemic, 7 to 9 October. The student companies had rates approximately twice those of the permanent party companies for the first three weeks, but by the fourth or fifth week the much reduced rates were approximately equal.

One student unit, Company A, USAECP, had a rate during the first three days of the epidemic which far exceeded that of any other unit on the post. In fact, this company, which contained less than three per cent of the post military popu-

lation, contributed 20 per cent of the excused from duty cases during the period 7-9 October

T E				Loc R F D case				un f 200 mw				h				
				F B a, 7.0 -6 N				9 7								
Permanent	Pos	Oct			Oct-6			Oct			Oct-6					
		Mean	Cases	No	Mean	Cases	No	Mean	Cases	No	Mean	Cases	No	Mean	Cases	No
Eng. Airc	TF			5	295	2	.8	2	0	0	0					
76 Eng		20			208	2		20	.5	3	9					
S	E	2	7	32.2	11		18.	232	2		256.5	2	8	22		
C A, C.D	Eng	00		9.0	408	22	53.9	22.5	3	30.	27.5			6	5	6
		0	2	22.2	0	2	9.5	20	.5	2	3.6	206		05		24
Sm E		509	5	2	2	6	12.0	516.5			519.5	9		6	0	
Med. C	Wt AH			0.6	6	3	25.2	5		2	5	3	5.8	5	6	9.7
		2			2		7	539.5	32	5	2	36.5	0	2		5
S	nt															
Ca	C	380		7	40	2		5	4.5	1	380	6	5	77		
Ca	EC	0		0.0	270.5	8	66.5	2.5	1		232	5	2	2	5	0
	E	32	6	2	30		6.2	9	6	20.5	8					
E	EC	2		12.6	348.5	3	8.6	3	05	6.6	1	7		32	1	3.1
	EC	0.5		5.0	5	5	2	66.	32	5	60	28.5	27	5		3.5
G	C	2		5	278.5		50.3	278	8	2	264.5	2		2		1
	ECR	27		9.3	2	0.5	5	3.5	87	4	288.5	1	3.5	2		1
	ECR	2			2	5	80.3	55	24	9	250.5	5	0.0	0	2	8.3
L	C	9	0	0.6	268.5		22.3	65.5	2	3.2	263.5			5	3	
	C	22.5		3.4	2		4.6	2	3.5	4.7	209	2		2		0
Stud. Off. Del. USAEC		666.5		6	40		13.5	2	3	36.	90	5	2	77		1
USMA Rep School		5		5.6.3	22.5		5.32	24	8	3	225.5		3	26		8
		ACOUS		5	4076.5		58.5	4065		5.0	996.5			38		
pe	mean	case	no	no	pe	mean	case	no	pe	mean	case	no	no	pe	mean	case

The causes of the exceedingly high rate in this company are not known. The unit had received personnel from Fort Carson, Colo., where an Asian influenza epidemic had been in progress during September. It is probable, however, that other student units had also received personnel from Fort Carson, which is a basic training post and, therefore, one of the chief sources of students. It is likely that there were undetected administrative and social causes which accounted for the high rate in Company A.

The marked drop in acute respiratory disease rates on week ends is of interest and probably indicates that a majority of the cases were relatively mild clinically, hence could delay their report to sick call for a day or so. The armed services have long been familiar with the week end decrease in sick visits. This, in most cases, does not indicate malingering during the rest of the week. It does represent either a genuine attempt by the individual to utilize his free week end time in self treatment and recuperation or a reluctance to seek medical aid and risk losing the free time. In either event, the individual is usually only mildly ill.

The same degree of illness during the week is often considered by the individual to be incompatible with military training and he, therefore, seeks aid. Frequently his opinion is shared



by the medical officer and he is hospitalized. In addition some of the mildly ill individuals who avoid the medical facility during the week end are much sicker by Monday and quite willingly report for sick call. This results in the familiar Monday peak. That this was true at Fort Belvoir is quite evident from figure 1.

### VACCINE EVALUATION

A few Asian influenza vaccinations had been given as early as 27 September but the vast majority were administered in the period 6 to 10 October in a program that was speeded up because of the upsurge in acute respiratory illness. Make up clinics were then held on 17 and 18 October for new arrivals and individuals who had missed the earlier vaccinations.

As a result of the haste with which the vaccination program was carried out recording of the individual vaccination was sometimes incorrect or omitted altogether. Because records were deficient it was found necessary to exclude some individuals from the vaccine evaluation. During the check of the vaccinations it was discovered that despite the efforts of the medical service more individuals had missed vaccination than might normally have been expected. In the two student companies subsequently studied approximately 30 per cent of the personnel remained unvaccinated as of 19 October.

Three student companies of the USAECR and three permanent party companies of the 91st Engineer Battalion were originally selected for vaccine evaluation study because they had high rates of acute respiratory disease. Subsequently one of the student companies had to be excluded from this part of the study because of its failure to report fully its gains and losses in personnel.

### MATERIAL AND METHODS

A complete roster of each study company along with the Asian influenza vaccination status of each individual was obtained. Arrangements were made for all personnel gains and losses and changes in vaccination status to be transmitted to the study team.

Army policy dictated that all military personnel receive the Asian influenza vaccine hence no attempt was made to set up control groups. Previous experience however had indicated that there would be an appreciable number of individuals who for various reasons would not receive the vaccine and therefore could subsequently be used as a control group of sorts. That the number of such individuals exceeded expectations has already been pointed out. The unvaccinated individuals as a group probably contained no more bias than would have been present in a volunteer control group.

The information obtained from the study companies along with information on cases obtained from the hospital was incorporated into modified life tables. The tables were so arranged that the experience of the groups could be divided into that which preceded and that which followed vaccination.

The analysis was made in two ways. In one, the vaccine was assumed to be effective immediately, while in the other the vaccine was assumed to be effective four days after administration. The effect of these assumptions is to penalize the vaccinated group inasmuch as antibodies against influenza do not usually develop to protective levels until about a week after vaccination.<sup>1</sup>

It has been pointed out that the incidence of Asian influenza, assuming from the initial laboratory results that the majority of cases were of this disease, was twice as high in students as in permanent party personnel during the early weeks of the epidemic, while with the waning of the epidemic the residual acute respiratory disease became equally distributed. The degree of proximity could have contributed to this difference. A major factor, however, was the time and completeness of vaccination. Because the student companies were vaccinated later and less completely than the permanent party companies, there were more unprotected individuals in the student companies at the height of the epidemic.

In preparing table 2, the vaccine was considered to be effective immediately upon administration. Both student companies and one of the three permanent party companies show evidence of vaccine protection even with this unlikely assumption. The other two permanent party companies show higher rates for the vaccinated than for the unvaccinated.

An analysis has been made in table 3 allowing a four day delay following vaccination before the vaccine was effective. With this more reasonable assumption it is possible to demonstrate protection in all five companies. Under these conditions, the acute respiratory disease rate in the unvaccinated group exceeds that of the vaccinated group by more than three and a half times in the students and one and a half times in the permanent party.

The occurrence of higher rates in the vaccinated than in the unvaccinated personnel of two of the permanent party units can be explained on the basis of time of vaccination. Almost all of these men were vaccinated at the height of the epidemic. Thus many cases occurred in these personnel before vaccine protection developed. By delaying the transfer between groups for four days many more cases are retained in the unvaccinated group thereby elevating its rate above that of the vaccinated and eliminating the previous unlikely relationship.

The use of the arbitrary four-day interval for the development of vaccine protection resulted in lower disease rates among the vaccinated in all five study companies. However, in the

TABLE 2 — Incidence of primary disease in five companies at Fort Belvoir, V. 70, October 6–November 1957, based upon the assumption that the Asian influenza vaccine was effective immediately

Vaccinated	Student			Permanent Party			
	Co. A USAECR	Co. K USAECR	Total	Co. B 91st Eng.	Co. D 91st Eng.	H/SCo. 91st Eng.	Total
Person-days	6115	2717.5	8832.5	3941	5620	5122	14683
Cases	24	9	33	13	34	11	58
Rate (Cases per 1000 person-days)	3.9	3.3	3.7	3.3	6.0	2.1	4.0
Unvaccinated							
Person-Days	3458	3937.5	7395.5	1447.5	256	1304	3007.5
Cases	61	42	103	7	1	1	9
Rate (Cases per 1000 person-days)	17.6	10.7	13.9	4.8	3.9	0.8	3.0

TABLE 3 — Incidence of cumulative primary disease in five companies at Fort Belvoir, V. 70, October 6–November 1957, based upon the assumption that the Asian influenza vaccine was effective four days after administration

Vaccinated	Student			Permanent Party			
	Co. A USAECR	Co. K USAECR	Total	Co. B 91st Eng.	Co. D 91st Eng.	H/SCo. 91st Eng.	Total
Person-days	5345	2270.5	7615.5	3362	4874	4501.5	12737.5
Cases	19	7	26	9	24	8	41
Rate (Cases per 1000 person-day)	3.6	3.1	3.4	2.7	4.9	1.8	3.2
Unvaccinated							
Person-Days	4228	4384.5	8612.5	2026.5	1002	1924.5	4953
Cases	66	44	110	11	11	4	26
Rate (Cases per 1000 person-day)	15.6	10.0	12.8	5.4	11.0	2.1	5.2

unvaccinated groups the effect was to raise the rates in the permanent party companies while lowering them in the student

companies This apparently ambiguous result is also explained by time of vaccination The transfer in the permanent party group occurred early in the epidemic and affected relatively more cases than in the student group where the transfer occurred later when the epidemic had already lessened in severity

### CONCLUSIONS

While the absence of adequately controlled conditions during this study prevents the establishment of scientifically acceptable conclusions the results do yield impressions to which some significance may be attached

The acute respiratory disease incidence rates of unvaccinated personnel exceeded those of vaccinated personnel in all study companies, when four days was allowed for the development of vaccine protection Inasmuch as the epidemic was shown to have been caused by the Asian influenza virus in the absence of other common factors the vaccine may be considered to have been responsible for the difference

### SUMMARY

An epidemic of Asian influenza occurred at Fort Belvoir, Va in October 1957 It began at approximately the same time as the Asian influenza vaccination A study of disease incidence and vaccine efficacy in recruit and permanent party personnel was made using the large number of inadvertently unvaccinated personnel as controls

The duration of the epidemic was approximately a month with the peak occurring in the first week A rapidly effected and efficient program of hospitalization undoubtedly contributed to shortening the epidemic Student acute respiratory disease rates were double those of permanent party personnel during the epidemic and approximately equal thereafter Depression of the rates on week ends was marked

Vaccine protection was suggested in the five units studied even though the data was arbitrarily arranged so that inadequate time was allowed for the development of antibodies following vaccination Acute respiratory disease rates in the unvaccinated student and permanent party groups were more than three and a half and one and a half times respectively those of the vaccinated groups

The higher degree of protection in the student than in the permanent party personnel was considered to be due to differences in time of vaccination The higher over all rates in the

students were considered to be due to greater exposure resulting from the closer proximity of the students to each other

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a d staff of D W tt Army H p l F rt B l V d Sfc C. H  
G odwin f W l r Reed Army I t r t f R arch W hngto D C.  
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#### ARE REFERENCE LISTS NECESSARY?

Op nions among authors and reader vary concerning reference lists appended to scientific articles The scien-  
tific editors are practically unanimous in agreeing th t they  
mean little or nothing to average readers rarely are the  
lists desired by teachers and specialists for filing purposes  
Some authors are sensitive about publication of references—  
espec ally when they contain their own names from one to  
many times! The lists imply that the author has studied each  
item nd h s d gested and recorded the pearls for benefit  
of his re ders However many authors will admit that a  
conscientious secretary has plucked them from the *Cumulative  
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which serves a large territory and mostly general practition-  
ers who want the mental pabulum boiled down

—EDITORIAL

Rocky Mou t in Med al Jo rn l  
p 1005 Oct 1957

# THE ADOLESCENT—A MEDICAL MISFIT

FREDEPICK C. BIEHUSEN *Major MC USA*

**N**O OTHER age group has received as little special attention as the adolescent. This important period of our lives is either omitted or glossed over in medical school. The average residency in both pediatrics and internal medicine serves the physician in training to no better advantage. Only recently has a medical school offered a postgraduate course in "Adolescent Medicine."<sup>1</sup>

Adolescents are an in between age group who fit neither into pediatrics nor internal medicine. The average physician has little interest or knowledge concerning this fascinating time of life. This is true in military medicine as well, where the sharp line of demarcation, the fourteenth birthday, will one day place the adolescent in the pediatric clinic (for which he thinks he is already too old) and the next day in the medical clinic (about which he may have apprehension because he sees few of his own age).

The ideal answer would be a clinic the adolescent could call his own, where he would be treated as an individual in a kindly and interested atmosphere.<sup>2,3</sup> It is likewise true that, in time, we should strive for separate adolescent inpatient units as well to provide well rounded medical care.

## THE NATURE OF THE ADOLESCENT

The adolescent is preoccupied with himself and his problems. He resists those who try to direct his life, yet is vulnerable to the person who shows interest, and responds with frankness and co-operation if he believes that genuine interest is being shown on his behalf.

Characteristically these young people show concern about growth and development, feel the need to be popular, show beginning criticism of adults and their behavior, feel a need for success, and a new realization of religion, look for independence, and yet retreat from their problems because of continued insecurity.

In seeing this new position they often deny the importance, continued dependency on, and authority of the parent. They thrive

on praise Directing this praise where it will do good helping them to happy and successful experiences, and exhibiting trust—all contribute to the confidence they need

The world of the adolescent is one of continual motion and competition They live strenuously work and play hard compete against each other and yet still have a very strong feeling of belonging with the gang A premium is placed upon physical appearance clothes complexion, and athletic and scholastic ability The adolescent appreciates honesty and frankness and *considers anything else a misuse of the trust they are willing to place in the physician*

### A CLINICAL APPROACH TO ADOLESCENCE

The physician dealing with the adolescent is in an enviable position He can offer the guidance solid advice and trust they seek He is also able to provide a positive approach in clinical relationships Adolescents prefer being told what they can do, not what they cannot do The adolescent worried about obesity will take to a regimen that stresses what he can eat rather than to a series of dietary don'ts "

Adolescents react more favorably to the physician and his advice when it is apparent they are responsible for their own care They prefer to be able to state their own problems and dislike being brought into the office in the magnificent wake of one or both parents The office should be free of toys and of the type of furniture that might give the impression that it is the office of a pediatrician If the physician is to create a good impression his own practice must be run in an orderly and punctual manner Allowing adequate time for each patient is important Neither party should appear or feel to be rushed Initial conversation directed to sports hobbies, and subjects other than medicine and school often foster friendship and serve to put the patient at ease

If the visit has initially been requested by the parents who desire to state their views such interviews are best accomplished on a day other than when the adolescent clinic meets In essence the adolescent should be allowed to seek his own medical care and not huddle in the shadow of the parent

In a busy clinic or practice it is difficult to schedule appointments for adolescents during the day when it will not interfere with school Evenings and Saturday mornings have become popular for this reason

Adolescence as a time of life is without well defined extremes It may well run from age 12 to age 21 No age limit therefore may be set for patients even in an adolescent clinic Roughly trying to group the appointments by age serves to foster patient confidence Our history taking should be both casual and complete The importance of the menstrual history and the taking

of the blood pressure should be explained. Vaginal examination will be necessary only rarely, and when really necessary is best done under anesthesia. It is a psychologically traumatic experience at which less information may be gained (because of the tension it produces) than if a careful rectal examination had been done. Rectal examination also should be fully explained beforehand, both to avoid fright and to ensure better relaxation.

Because the adolescent is more willing to place his trust in one physician, referral to one consulting specialist after another is undesirable. A bewildering succession of visits to one physician after the other often raises doubt that any of them know what they are talking about, and dilutes the valuable patient-physician relationship. When consultation is necessary, the consultant, if possible, should come to the patient in the office of the clinic physician. This fosters the feeling that the adolescent and his physician are the important individuals concerned.

### COMMON PROBLEMS OF THE ADOLESCENT

In successfully carrying out relationships with the adolescent the practitioner must at times assume the mantle of the pediatrician, dermatologist, orthopedist, gynecologist, internist, and psychiatrist. Some of the major causes for concern are discussed briefly below.

**Growth** The radiological evaluation of bone age is often helpful in discussing this problem. If the bone age is normal the patient will usually either catch up with a growth spurt or slow down. The short, chubby adolescent is usually one who has not yet begun the adolescent growth spurt. An increase in leg length is often the first clue that such a period of growth is under way. In the absence of hypothyroidism and familial traits, growth will usually progress satisfactorily. An honest discussion about familial traits and the growth processes often is all that is required.

**Obesity** If the patient can be acquainted with the relationship of prepubertal chubbiness and growth, and if organic disease can be ruled out, it is often possible to guide adolescents through this period without drug or dietary regimens. Overeating as an emotional outlet must be considered. If, after careful investigation, dietary control seems indicated, stress the foods to be encouraged and do not play up the don'ts of dieting. Make the diet appealing. Ensure adequate exercise and physical activity. Obesity and concern over a poor appearance go hand in hand. The determination of the patient may produce more gratifying results than the physician's counsel.

**Sexual Maturation** Puberty and sexual maturation are often causes for concern. Early or late development of secondary sex characteristics, even though well within the normal range, may cause severe emotional disturbance, especially today when so



much emphasis is placed on anatomic evidence of sexual maturity. Reliable signs that all is progressing well are, in the female budding breasts in the male penile changes and in both the axillary and pubic hair development and the changes in pigmentation associated with puberty. Frank discussion with the patient, stressing the variability of the time of onset of these changes, often has the desired effect in calming apprehension.

**Acne.** Even though acne is a relatively minor complaint to the physician it is of importance to the patient because it deters from an otherwise perfect appearance. Acne has been responsible for withdrawal from school activity, decreased popularity socially, and scholastic failure because of the self-consciousness it engenders. Cleanliness and a good lotion are the basis of treatment. Mild dietary restriction may be indicated. It is well to remember that the adolescent patient with acne may well be using this as an entry for a more serious complaint.

**Gynecomastia.** Gynecomastia usually presents as a sometimes tender button-shaped swelling under the areola. It is said to be experienced by approximately 80 per cent sometime during adolescence. A simple explanation that this is normal is usually all that is necessary. The other less common type results in a generalized enlargement of the affected tissue giving the appearance of true breast enlargement. Here size is the chief concern and it may be necessary to enlist the aid of the plastic surgeon. Care should be taken to differentiate between Klinefelter's syndrome with its associated impotence.

**Failure in School.** School is to the adolescent what business or a profession is to the adult. It is his job. Apprehension over school work may be the underlying reason for psychosomatic complaints. This can often be ascertained through the simple expedient of studious listening and questioning during the visit. Standard writing and arithmetic tests should be a routine part of the work-up. A few students who have reading difficulty do reasonably well in school. Specific language defects and marked variance between chronologic and mental ages must be investigated.

**Psychosomatic Complaints.** Low back pain, headache, fatigue, precordial pain, or tachycardia may be the masked presentation of emotional stress at home, in school, or in relations with the patient's peers. Do not jump to the conclusion that the cause is organic, but do not label the disorder psychosomatic until the organic has been ruled out. The labile blood pressure of the adolescent (a pressure up to 140/90 mm Hg may be considered normal) may be responsible for a mistaken diagnosis of hypertension. Familiarity with blood pressure techniques is important in avoiding the labile response and is a good argument for the routine taking of blood pressures in pediatric practice.

**Ulcerative Colitis** The responsibility of the physician is primarily that of offering advice, over all guidance, and direction of the therapeutic program. Basic understanding of the patient is the cornerstone of the therapy. Diet, antibiotics, steroids, and surgery all seem to have an indicated role in therapy. The role of the emotions cannot be denied and must be carefully considered in evaluation of the patient.

**Dysmenorrhea** A frank and practical discussion often pays dividends in helping young women with dysmenorrhea. Sometimes the philosophy of menstruation is learned solely from the mother who may give the impression that the physiologic process is meant to be painful, and dysmenorrhea is used as a means of obtaining sympathy. Is painful menstruation a feminine response to the tensions of adolescence? In differentiating primary from secondary dysmenorrhea, the administration of 1 mg. of estrogen daily for 21 days, starting on the first day of the period, with a resulting pain free period is good evidence that the difficulty is primary or nonorganic dysmenorrhea. Cramping may be normally associated with menstrual periods, or may herald the onset of ovulatory cycles. Menorrhagia, even though a physiologic alteration, is best discussed with the gynecologist. It is again emphasized that careful thought should be given before performing pelvic examination in the adolescent female.

A graphic record of the menstrual cycle is often helpful in understanding the physiologic nature of menstruation. Emotional evaluation is important. Does the onset of menstruation represent the end of childhood? Does the patient resent growing up? Would she rather be a boy?

## DISCUSSION

It is becoming apparent the adolescent receiving his medical care in the service together with many of his peers in civilian life, has no readily available source of sympathetic medical care. The peculiarities of nomadic service life often make serial follow up difficult. To date, few adolescent outpatient clinics are in existence. Conversation with those pioneering the adolescent movement reveals that their experience came from actively working with the adolescent. Philosophies and techniques were developed as a result of experience. A few actively interested service physicians could stimulate interest in adolescent medicine throughout the armed services. Careful consideration given to existing physical facilities usually will reveal an adequate plant for successful operation of an adolescent clinic.

The physician with a specialty may doubt the wisdom of working in the adolescent clinic with its atmosphere of "general practice," and the general duty medical officer may express doubt in his ability to handle some of the specialized problems that occur. The relatively small number of patients seen is often

misunderstood as meaning that adolescent medicine is unrewarding. It is not volume of patients seen but rather the standard of care given the individual that denotes the successful adolescent clinic.

Inasmuch as the average training program in both pediatrics and internal medicine currently makes no provision for training in adolescent medicine, joint operation of the clinic for adolescents would benefit the adolescent patient and provide excellent training for the resident physician.

Local interest has resulted in the formation of an adolescent clinic at this hospital. The clinic began operation in March of 1958 and has been incorporated into the teaching program of the pediatric service. It is thought to be the first such clinic in the armed services.

Communication on this subject between pediatricians in the service should be fostered to stimulate interest in the adolescent. If present efforts result in the formation of a section for military pediatrics within the American Academy of Pediatrics, a fertile meeting ground for discussion will be provided. The problem of adolescence and other mutual problems of pediatrics in the Armed Forces would benefit.

#### SUMMARY

Adolescent medicine is a neglected field and to meet the special problems and complaints of the adolescent there is need for the establishment of independently operating adolescent units in service hospitals. Co-operation between the pediatric and medical services could result in teaching material beneficial to both. An adolescent clinic is now in successful operation at this hospital.

ACKNOWLEDGMENT The author wishes to thank Dr. J. Rowell Gilghrist for the Adolescent Unit at the Boston Children's Medical Center for his efforts during preparation of this article.

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# AN ECONOMICAL SUPPORT TO MAINTAIN A FUNCTIONAL FOOT POSITION IN BUCK'S EXTENSION

GEORGE E. OVER, Jr. Major MC USA  
THOMAS J. ERWIN

**G**URDON BUCK<sup>1</sup> devised a skin traction system in 1907 that is an excellent appliance for relief of pain caused by muscular spasm or other conditions that require partial immobilization with simple traction for short periods of time. Buck's extension is applicable to a larger number of problems than any other one form of traction.

One technique for application of Buck's extension consists of placing the patient in a supine position with a firm mattress for support beneath the injured leg. The extremity is shaved and prepared by painting from knee to malleoli with benzoin or Ace Adherent\*. Two strips of moleskin adhesive of suitable width are applied longitudinally to the inner and outer aspects of the extremity, extending from just below the knee to 8 inches beyond the sole of the foot. The moleskin strips are held in place by the Ace Adherent and an elastic bandage wrapped circularly from the knee to malleoli. An alternate method consists of placing thin strips of sponge rubber against the leg to prevent slipping, and over this the moleskin strips are compressed by 4 inch elastic bandages. After completing the leg, a 7 inch canvas strap, 1 inch wide and with a buckle at each end, is tacked to a wooden block 2 inches wide by 4 inches long and with a 1 inch hole in the center. A traction rope is passed through the hole and over a pulley attached to the foot of the bed in a direct line with the affected limb. Weights of 5 to 10 pounds are added to the traction rope. The weight and pulley system is completed when the distal end of each moleskin strip on the leg is folded on itself to form a tongue which is adjusted and fastened into the canvas strap buckle on each side of the wooden block.

The wooden block is wide enough across the foot to release pressure from the malleoli but does not have enough longitudinal

From Irwin Army Hospital, Fort Riley, Kansas.

\* Ace Adherent is a trademark of the American Medical Supply Company, Inc., 1000 North 10th Street, Minneapolis, Minnesota. Stock Number 6510-200-0160. Adhesive is liquid urethane.

length along the sole of the foot to prevent plantar flexion contractures (fig 1) In addition a doughnut pad usually is required to relieve pressure on the heel against the firm bed A prolonged



Fig 1 B k xten so th a d u tho t po t al supp t d m t at g foot drop a d b l pres ur app rat u th ut foot upp t

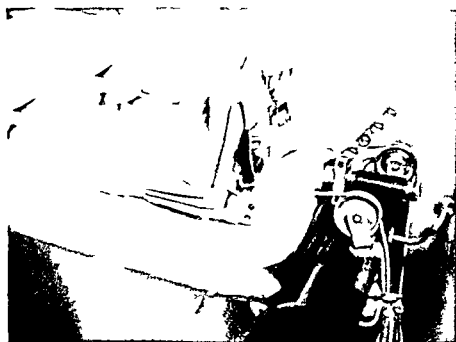


Fig 2 B k so u th al m m foot upp rt d m st t g l t on f h l d 90 foot p t n.

positional foot drop can result and become a fixed deformity. The proper 90 degree functional position of the foot is maintained poorly with pillows or wooden blocks or even a sling over the foot pulling toward the patient's head.

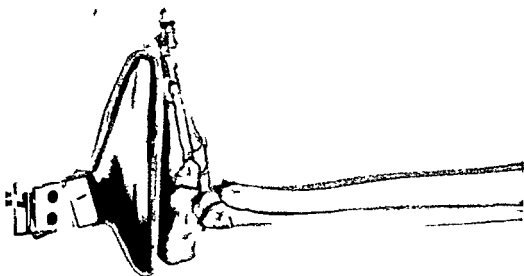


Figure 3. Brace showing relationship to bones in the foot and leg.

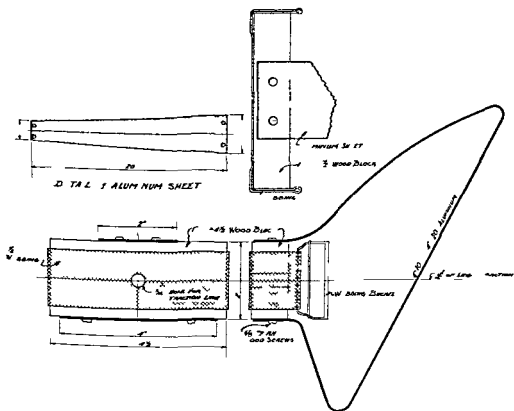


Figure 4. Working diagram for manufacturing brace.

To prevent foot drop and calcaneal ulcers during traction a practical foot support is made from an aluminum metal strip 4 inches wide and 20 inches in length Of 10-gage weight it is bent into a C shape with the long flat edge against the patient's foot and the two curved arms of the C fastened to the upper and lower sides of the wooden traction block (figs 2 3 and 4) The long curve of the C maintains the foot at 90 and the lower end of the C elevates the heel from the bed and prevents cutaneous pressure lesions Adhesive padding is used to cover the surface and edges exposed to the patient (fig 5)

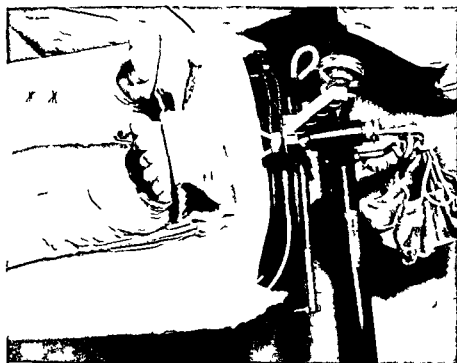


Fig 5 Buck's traction with aluminum foot support built up with padding of plaster padding attached to aluminum strip to wooden traction block.

The light aluminum material is easy to obtain, easy to cut and costs approximately 15 cents for each foot support. It is strong enough to maintain the foot in functional position and can be used over and over again simply by changing the adhesive padding against the patient's foot. It is believed that this is an economical and practical foot support to maintain a functional position during Buck's extension.

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## SERVICE ARTICLES

# MILITARY ASPECTS OF THE BIOLOGICAL EFFECTS OF RADIATION

**NATHANIEL I. BERLIN** *Lieutenant Commandant USNR R*

**T**HIS report has been prepared to provide a review of the broad field of radiobiology as it applies to military problems.

There are some data available for man which are not particularly satisfactory. There also is a large volume of data obtained from laboratory and weapons test studies in experimental animals. It manifestly is not possible to cover within the scope of this document the entire field of radiobiology. This report attempts to review the problems; for details it is suggested that the reader consult the general and specific references.

In many respects the physical weapons test data have been collected for the purpose of evaluating the hazard of ionizing radiation to personnel. Except at very high dosages (10 000 r and greater), ionizing radiation is without effect on ordinary material other than radiation dosimeters and photographic film. The basic purpose of this report is to provide some guidance in the use of physical data for the estimation of personnel hazard. In many, if not most, instances the needed correlation between exposure dose and clinical findings is lacking because of insufficient data.

**Source of Data** The primary sources of pertinent medical radiobiological information are

- 1 The evaluation of the results of the Hiroshima and Nagasaki experience by the Atomic Bomb Casualty Commission <sup>1</sup>
- 2 The evaluation of the results of the accidental exposure of the Marshallese during Operation CASTLE <sup>2</sup>
- 3 Accidents in atomic energy laboratories <sup>3</sup>
- 4 Clinical radiotherapeutic experience

In addition, there is a large volume of experimental animal data from which certain inferences regarding man may be drawn, but which cannot be applied directly. In general, animal experiments indicate the pattern of response that may be anticipated

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in man, but are not an ideal source of information. Significant differences in details particularly quantitative preclude direct extrapolation to man. In fact, all sources lack certain pertinent critical information.

As an example review of the problems associated with the calculation of radiation dosage at Hiroshima and Nagasaki result in the conclusion that at Hiroshima neutron effects might predominate while at Nagasaki nearly all the dosage is due to  $\gamma$  rays. Aside from the difficulties associated with estimating the flux and energy spectrum of neutrons and the  $\gamma$  ray dose there is considerable difficulty in assigning to a given location a number for dose because of the rapid decrease of the dose with ground distance both for neutrons and  $\gamma$  rays. This is without consideration of an estimate of shielding factors. As will be discussed later the biological effectiveness of neutrons may be greater than  $\gamma$  rays. Comparison of the results obtained at Hiroshima with those at Nagasaki should make some provision for this difference. But in addition the flux and spectrum for a given location are so poorly known that in all probability quantitative data purporting to relate lethality to dose are of dubious value.

The dosimetry problems associated with the exposure of the Marshallese make it difficult to determine precisely the  $\gamma$  ray dose.<sup>2</sup> The data were insufficient to permit even an attempt to be made to estimate the skin dose resulting from low energy  $\gamma$  rays and  $\beta$  radiation. The many problems and uncertainties involved in the dosimetry of accidents in atomic energy laboratories are pointed out in a description of an accident at the Argonne National Laboratory.<sup>3</sup>

**Types of Hazard** The personnel hazard may be divided into immediate and late considerations. The immediate hazard is that involved in the production of acute effects principally lethality, acute radiation illness or skin lesions. The long term problem is that of the late effects; this involves both the individuals concerned and through the genetic changes produced by radiation their progeny for many generations.

**Sources of Radiation** There are two separate sources of ionizing radiation to be considered. These are

1 *External  $\gamma$ ,  $\beta$  and neutron radiation* For residual radiation this is a combined  $\beta$  and  $\gamma$  radiation; for initial radiation neutrons are an additional source of ionizing radiation.

2 *Internally deposited radioactive materials* For military considerations this is a problem associated with fallout.

### EXTERNAL RADIATION

External radiation constitutes a potential hazard to personnel from the moment of detonation of an atomic weapon. The initial

radiation consists of  $\gamma$  and neutron radiation, propagated for large distances in air. In addition, within the cloud there is  $\beta$  radiation, but it is difficult to conceive of a situation where  $\beta$  radiation will constitute a personnel hazard before fallout occurs. While falling and after completion of fallout, the external radiation consists of both  $\beta$  and  $\gamma$  radiation.

**Dosimetry** From the standpoint of estimation of personnel hazard from external radiation, the basic necessary physical data are

- 1 The type of radiation, whether it be  $\gamma$ ,  $\beta$ , neutron, or some combination of these
- 2 Knowledge of the energy spectrum and flux
- 3 Source geometry

**Units of Dose** There are several units of radiation dose currently employed:

1 Roentgen—defined as the quantity of  $x$  or  $\gamma$  radiation that produces in 1 cm<sup>3</sup> of air at STP conditions 1 e.s.u. of charge of either sign.

2 Rep (roentgen equivalent physical)—that quantity of ionizing radiation which results in an absorbed dose in any material at the site of interest that is equivalent to that obtained from 1 r of  $x$  rays, this quantity is usually taken as 84 ergs for 1 gram of air, for soft tissue this is 97 ergs/gm tissue. This unit is independent of the type or energy of the ionizing radiation.

3 Rad—that quantity of ionizing radiation which results in the transfer of 100 ergs/gm to any material. This is a recently adopted unit. It can be seen that for soft tissue it is almost equivalent to the rep.

4 Rem—roentgen equivalent mammal (man) to be defined later.

From these definitions it is seen that the roentgen is a unit applicable only to  $x$  or  $\gamma$  radiation, while the rep and rad are independent of the source type and energy.

**Consideration of Depth Dose Curve and Correlation with Biological Effect** The effect of ionizing radiation is dependent primarily upon the dose absorbed in tissue, *not* the dose measured in air. The basic problem is a determination or a calculation of the absorbed dose in tissue. This probably is best approached through the use of a depth dose curve. A depth dose curve is a graph of the relative amount of ionization produced at various depths in the body or some other absorber. Depth dose curves have had extensive application in radiation therapy and in radiobiological research. It is this experience that makes possible the quantitative prediction of biological effect from a depth dose curve.

For the range of  $\beta$  particle energies encountered in fission products, maximum penetration into tissue is of the order of millimeters, while for x and  $\gamma$  rays and neutrons the degree of penetration can vary from a few mm to those which traverse the entire body. As a consequence of the change in absorption coefficient with x ray energy, penetration into the body varies with the energy. For example, for 50 kvp x rays the dose delivered to tissues deeper than 2 cm is small compared to that at the skin surface. The skin surface dose to produce an LD might reasonably be expected to be greater for 50 kvp x rays than for 250 kvp x rays because the 50 kvp x rays may be considered to produce a skin burn while with 250 kvp x rays a relatively uniform dose throughout the body is produced. For dogs it has been shown that below 175 kvp the air exposure LD dose increases rapidly to 6 000 r at 50 kvp.<sup>7</sup>

The  $\beta$  particles arising from fission products constitute a source of radiation only for the skin and in sufficient quantity, produce a condition known as a beta burn which can be lethal. The two principal considerations in the evaluation of the hazard of  $\beta$  radiation to the body are

- 1 Dose to skin and
- 2 Area of skin involved

For example, it has been determined that the LD for  $\beta$  radiation to the entire body varies from 1 500 rep (baby rat) to 30 000 rep (pigs) while the same dose range delivered to a small area of skin e g 1 cm<sup>2</sup> will not result in death but will produce only local changes in the skin. The relatively low LD for  $\beta$  radiation for the baby rat is probably due to the fact that for such small animals there is significant ionization beneath the skin and while this is not uniform total body irradiation a considerably greater percentage of the tissues are irradiated than in larger animals.

The lethal dose for  $\beta$  radiation of man is not known. Animal studies indicate that the total integrated dose to produce 50 per cent lethality may be directly proportional to the body mass. Extrapolation to man yields an LD for  $\beta$  radiation of approximately 40 000 rep which is not in keeping with other data and should not be used for personnel hazard calculations. On the other hand from another line of approach the  $\beta$  radiation LD dose is calculated to be approximately 5 000 rep. The latter appears to be a more acceptable value and is comparable to the LD for dogs for 50 kvp x rays but it is unestablished and must be considered only as an estimate of questionable value arrived at by extrapolation from animal data.

X rays and neutrons of sufficient energy produced ionization throughout the body resulting, when applied in sufficient quantities, in acute radiation illness

**Dosimetric Methods** In general, and for most peacetime applications, film badges are the most common dosimeters in current use Varying sensitivity to various types of ionizing radiations precludes their use for precise dose measurements in mixed radiation fields In addition, at weapons tests, where mixed radiations make the physical measurement of dose difficult, biological dosimeters have been used Generally, mice are placed at various distances from the point of detonation in suitable containers to protect against the effects of thermal radiation and blast Then the effects of the ionizing radiation are measured by one or more biological end points The biological end points used are<sup>9</sup>

- 1 Mortality (30 day)
- 2 Change in weight of the spleen and thymus
- 3 Depression of red cell formation, as measured by the incorporation of radioactive iron into red cells
- 4 Change in weight of the gastrointestinal tract
- 5 Survival time (in the supralethal dose range)

The results then are compared with those obtained with x rays in similar animals under laboratory conditions The results are expressed not in terms of the mixed bomb ionizing radiation, but that at a particular station, the total effect of the ionizing radiations received is equivalent to a particular dose of x rays

Chemical and glass dosimeters also have been developed, but are less widely used<sup>5</sup> It is possible that because of their relative simplicity, chemical dosimeters will become more widely used Gamma radiation is generally best determined by some type of ionization chamber, although if suitably calibrated, photographic film may be used

The measurement or calculation of neutron dose is more complex<sup>10</sup> Fast neutrons are slowed down in tissue by elastic collisions, principally with hydrogen, resulting in recoil protons

Capture reactions predominate with thermal neutrons these are the  $n, p$  reaction with  $N^{14}$ , resulting in the emission of a 0.66 mev proton and the  $n, \gamma$  reaction with hydrogen, resulting in the emission of a 2.2 mev  $\gamma$  ray Calculation of the dose at the surface and the depth dose curve thus depends upon the flux and spectrum Suitable ionization chambers in a phantom also have been used to determine the depth dose curve

Recently it has been observed that within the ground range of interest, the bomb neutron spectrum is relatively constant Thus, a calculation of dose due to the entire bomb neutron spectrum can be carried out from the measurement of the flux of a single energy region

The dose due to  $\beta$  radiation is best determined by a suitable thin walled ionization chamber  $\beta$  radiation can be considered to arise from two sources

a  $\beta$  particles emitted from fission products upon the surface of the ground

b  $\beta$  particles emitted from fission products that contaminate the skin or clothing

In the first case, the individual is in a field of  $\beta$  radiation, and aside from consideration of the protection due to clothing and the attenuation of the flux with height from the ground surface may be considered to be in a field of uniform  $\beta$  radiation. In the second case however there is in addition the  $\beta$  radiation arising from hot particles contaminating the skin or clothing and producing a local area of intense irradiation.

Directly measured depth dose curves furnish the most satisfactory approach to the prediction of biological effect. The use of small ionization chambers in a phantom appears to be satisfactory. This type of measurement consists in the placing of small ionization chambers at various depths in a Masonite phantom. After exposure the readings of the ionization chambers are plotted as a function of the depth from the surface of the phantom. This is a directly determined depth dose curve for the particular source source geometry and receiver. For neutron irradiation a first collision dose calculation with an estimate of the attenuation due to depth is a good approximation.<sup>1</sup>

#### Significance of Air Dose Skin Dose and Mid line Dose from X ray Radiation

*Collimated beam source geometry* Considerable confusion has arisen from failure to stipulate how the dose was measured. This is because from the same narrow collimated x ray flux in air these three quantities air dose skin dose, and mid line dose can and do differ significantly. Air exposure is the dose measured in free air that is without back scatter. Skin dose is the dose measured with back scatter that is the ionization chamber is placed at the surface of the body. Mid line dose is the dose either measured in a phantom with size and radiation absorption characteristics similar to the biological object under consideration or calculated from a knowledge of the energy spectrum and absorption constants. The skin dose is higher than the air exposure dose due to back scatter. The mid line dose is a function of the energy spectrum and body size and is usually less than the air dose and skin dose.

The relationship between air dose and mid line dose is dependent upon the source and receiver geometry and with low energy x rays on the absorption constant. Because there is considerable variation with energy in the absorption constant

the ratio air dose/mid line dose can vary considerably. For example, from weak x rays (below 50 kvp) the mid line dose may be negligible as compared to the skin dose, in which case the ratio mid line/air dose will be very low while in the  $\gamma$  ray region this ratio may approach 1. It can be seen readily how failure to stipulate the measurement conditions may lead to considerable confusion.

*Infinite plane source geometry* For the case of radiation in a fallout field, i.e. infinite plane source geometry, the relationship between air dose, skin dose, and mid line dose is different. Direct observation of the hard  $\gamma$  radiation component of a fallout field in a phantom Masonite man indicates that within the error of measurement there is no appreciable change below 3 cm with depth, that is, the  $\gamma$  radiation depth dose curve is relatively flat, and equal to the free air exposure in roentgens, as measured by a thick wall ionization chamber.<sup>2</sup>

Which of these three measurements—air, skin, or mid line dose, is the most satisfactory? In all probability there is no single measurement which will be satisfactory in all cases. For weak x rays (below 50 kvp) certainly the mid line dose is unsatisfactory while the skin dose or air dose may be misleading if it is not realized that this radiation is essentially body surface or skin radiation. The measurement to be used depends upon the biological end point under consideration. The mid line dose is to be used when total body irradiation, acute radiation illness, and lethality are under consideration, as it affords the best correlation between dose and effect. However, for consideration of the skin beta "burn" hazard it is necessary to know the dose to the skin. It thus is apparent that a single measurement or calculation is not satisfactory for all cases. For military operational purposes it has not been determined if it is necessary to know both the skin and mid line dose.

For the fallout field where there is a combination of both  $\beta$  radiation and weak x rays and  $\gamma$  rays the use of the phantom Masonite man probably defines the problem most satisfactorily because the results permit an evaluation of (1) the dose to skin and (2) the whole body dose. The results may be expressed as a ratio ( $\frac{\beta}{\gamma}$  dose ratio).<sup>2</sup> Experimentally this measurement

has been carried out in a limited number of conditions. Values of the  $\frac{\beta}{\gamma}$  dose ratio varying between 2.5 and 28 have been ob-

served at field tests.<sup>11</sup> Dale has worked out on a theoretical basis the variation with time of this ratio up to 400 days. Initially the ratio of surface dose to mid line dose is high, approximately 15 or 20, decreasing to a minimum of about 2 at 10 to 20 days.<sup>11</sup>

CONCEPT OF RBE (RELATIVE BIOLOGICAL EFFECTIVENESS)<sup>1</sup>

With the availability of various types of ionizing radiation it early became apparent that prediction of the effects of a given physical dose was inaccurate when the biological effects of heavy ionizing particles were compared to those of x rays. This was particularly true for external neutron irradiation. Initially, neutron doses were measured with a Victoreen ionization chamber and in units of n. One n is the neutron flux to produce a reading equivalent to 1 r in a 100-cm<sup>2</sup> Victoreen ionization chamber. Recently it has been confirmed that 1 n = 2 rep.<sup>1</sup> The biological effect of 1 rep of neutrons is greater than would be anticipated from 1 rep of  $\gamma$  radiation, and to rationalize this discrepancy the concept of relative biological effectiveness (RBE) was introduced. When compared to x rays, and for equivalent biological effect, the flux required of any ionizing radiation is the product of the RBE and the dose delivered in rep unit flux. It should not be inferred that RBE is used only in connection with neutrons. The RBE has been determined for  $\alpha$  particles, protons, and  $\beta$  particles, and within the spectrum of x and  $\gamma$  rays.

RBE is not a simple concept; it depends upon

- a. Type and energy spectrum of ionizing radiation
- b. Biological end point measured
- c. Dose and dose rate

It is particularly when different biological end points are considered that a large range of values for RBE are encountered. With the development of the concept of RBE, a new unit, the rem (roentgen equivalent mammal (man)) came into use. The rem is the product of the absorbed dose (in rep) and the RBE for the particular type of ionizing radiation used and biological end point measured.

An explanation for the fact that from a given physical dose the magnitude of the biological results varies probably is related to differences in linear energy transfer.<sup>1</sup> Basically, it has been observed that for the same physical dose, as the linear energy transfer (or the density of ionization per unit path length) increases, the magnitude of the biological effect goes to a maximum. A rigorous discussion of the mechanisms involved is not attempted here. Then for the heavy charged particles ( $\alpha$  particles and protons) the biological effect generally will be greater than for  $\gamma$  rays. Because most of the energy transmitted to tissues from neutrons is through the ionization produced by recoil protons, it would be anticipated that for a given physical dose (ergs/gm) neutrons would produce a greater biological effect than  $\gamma$  rays. For military medical purposes, an important RBE, but not the only one desired, is the RBE for bomb neutrons for acute lethality. Field tests indicate that this particular RBE is approximately 1.7 in mice.<sup>1</sup> For

60 inch cyclotron fast neutrons with a different RBE in dogs is approximately  $10^{10}$ . This and estimate of 1.7 may be high, and that the KBF for man for bomb neutrons may be 1.0 or less.

### DESCRIPTION OF ACUTE RADIATION SICKNESS

**Symptomatology** For military medical purposes the radiation syndrome should be considered from the following standpoints

- 1 Symptomatology and relationship of symptomatology to continued military effectiveness
- 2 Incidence and duration of symptoms as a function of dose
- 3 Incidence of lethality as a function of dose

For man the most useful sources of information are (1) the evaluation by the Atomic Bomb Casualty Commission (ABCC) of the Hiroshima and Nagasaki experiences<sup>1</sup> (2) experience derived from clinical radiation therapy<sup>19, 20</sup> and (3) the evaluation of the Marshallese exposed in March 1954.<sup>2</sup> Unfortunately all these sources of information contain basic uncertainties precluding good quantitative conclusions.

The Hiroshima and Nagasaki data are valuable for a description of disease, but cannot be correlated closely with dose because the dose is not known nor are estimates of the dose good. The clinical radiation therapy experience is complicated because most is partial body radiation; in addition, it is complicated seriously by the underlying disease for which the patient is receiving therapy. Furthermore many patients have imparted to them some degree of awareness of nausea and vomiting as possible complications of radiation therapy, making this symptom difficult to evaluate. The knowledge gained from the study and treatment of the Marshallese also is complicated by uncertainty as to the dose received and the effect of a changing dose rate.

The situation is such that for the acute radiation syndrome, the symptoms encountered can be described but evaluation in relation to dose more importantly quantitative evaluation as to incidence, particularly in the range from no symptoms to 50 to 60 per cent of individuals symptomatically affected is not available. There also is no information available for the case of protracted radiation other than that obtained from the accidental exposure of the Marshallese.

The earliest symptoms are nausea and vomiting generally occurring within 6 hours after a single acute whole body penetrating  $\gamma$  ray exposure. Hereafter in the discussion, it is implied that the air dose figure mentioned does not include



scattered soft  $\gamma$  radiation. The incidence of nausea and vomiting as a function of dose is not well known. Probably below 50 to 100 r (air exposure) there are no symptoms and above 250 r to 300 r there is 100 per cent involvement but between no involvement and 100 per cent involvement the data are meager.

The sickness dose for 50 per cent of the population exposed is estimated as 150 r. In a study of a small group (about 20 patients) treated with 200 r (skin dose) unilateral almost whole body radiation exposure nausea and vomiting was noted in approximately 30 per cent.<sup>4</sup> In a second study of 30 patients exposed to a total air dose of 200 r with 100 r delivered to each side of the body 27 patients (90 per cent) were symptomatic. In 17 patients the reaction to radiation included vomiting. Of the Marshallese exposed to 175 r (air dose) over a period of approximately 46 hours with 75 per cent of the dose delivered in 36 hours nausea was noted in two thirds and vomiting and diarrhea in 10 per cent. At doses below 200 r there are no additional symptoms.

When both nausea and vomiting exist it should be presumed that such individuals are not capable of satisfactorily performing a military task. There is no information on the capability of man to perform work following an exposure to radiation sufficient to induce these symptoms nor is there adequate information as to the duration of these symptoms. Other clinical states involving nausea vomiting and diarrhea generally are associated with malaise and lassitude sufficient to prevent the carrying out of useful physical work. In addition the unevaluated and unknown degree to which individuals are motivated may play an important role. For the present the assumption of inability to perform a task probably is the best that can be made. The time required for recovery from these symptoms to full working or even partial working capability is not known possibly a few days are sufficient.

At higher dose levels additional manifestations of radiation sickness appear generally after a latent period of a few days. Because of the scarcity of data it is difficult to describe the precise time course of the onset and extent of involvement although various tables have been prepared in general having their origin in the Hiroshima and Nagasaki experiences.

Following the initial nausea and vomiting there is a latent or asymptomatic period varying from 1 to 3 weeks at 200 r to perhaps of the order of 1 week in the mid lethal range (400 to 500 r). Following the asymptomatic period at 2 to 4 weeks after exposure malaise and loss of hair (epilation) occur and small hemorrhages (petechiae) appear in the skin and mouth. Ulcerations occur in the mouth with symptoms similar to those of a sore throat plus bleeding from the gums. Similar ulcerations

in the bowel result in diarrhea. These complications are associated with alterations in the blood clotting mechanisms and a leukopenia. In the more heavily exposed (within the lethal range) anorexia, weight loss, and fever become the prominent symptoms. The red blood count decreases and the symptoms become more pronounced leading to death. Analysis of the Japanese experience indicates that percentage lethality can be correlated with lowest white blood count at particular times. In the survivors there is a variable period during which recovery takes place. In the range of moderate to marked symptomatology recovery to the point of being able to perform usual tasks may be of the order of 3 to 6 months or even longer.

At supra lethal doses 1500 r or greater central nervous system alterations have been observed in monkeys.<sup>21</sup> At very high doses (10 000 r or greater) delivered in less than an hour death may supervene during the irradiation or within a few hours. In monkeys lethargy, convulsions, and other neurologic manifestations occur. No data are available for man in this dose range.

At present it is not possible to predict for a given air dose for either unilateral exposure or for infinite plane source geometry the percentage lethality. It is recognized that for unprotected exposure in a fallout field there is received a combined  $\beta$  and  $\gamma$  radiation. Consideration of the biological effect of this type of mixed radiation is not possible at present. Probably below 200 r air dose there will be no lethality or at most a few per cent, while above 700 r there will be few survivors.

Where in this range the  $LD_{50}$  falls is open to question. By convention it has been set at 400 to 450 r (with an unspecified source and source geometry) but this is not fixed. Furthermore, the shape of the mortality versus dose curve is not known for man. In experimental animals this shape has been determined in a large number of experiments. A convenient method of expressing the result is the probit transformation, as this transformation results in a straight line. It must be pointed out, however, that these studies in animals, except for a few such as those carried out in mongrel dogs, have been conducted with pure bred laboratory animals of the same age. To postulate similar results from a probit transformation in man is not reasonable. In addition, the effect of changing the source geometry is not known for man although it would be expected that a change from unilateral to bilateral exposure or to infinite plane source geometry would produce a significant decrease in air  $LD_{50}$  dose as it does in the pig.<sup>22</sup> The original analyses of the Hiroshima and Nagasaki data and speculation lead to the adoption of 450 r as an  $LD_{50}$ . The experience gained from the Marshallese suggests a lowering below 450 r.

It should not be thought that these indicate basic differences the original figures derived from the Japanese data are subject to considerable error with regard to dose and are for unilateral single short duration radiation while the Marshallese data result from a more protracted radiation with an infinite plane source geometry plus an unknown quantity and unknown effect of  $\beta$  radiation to the skin and from the opinion that the dose received was on the borderline of lethality (50 to 100 r more would produce some mortality) Recent review of the Japanese data in the light of newer weapons test data suggests an increase of the LD<sub>50</sub> to approximately 650 r (air dose)

**Current Therapeutic Concepts** As a basis for discussion it must be presumed that at present there is no specific curative treatment for the acute radiation syndrome in man For the experimental animal there are a number of modalities used either before or after irradiation leading to reduction in acute mortality These are (1) radiation in the hypoxic state (2) transfusion of bone marrow or spleen or homogenates of bone marrow or spleen (3) various chemicals *e g* cysteine (4) antibiotics and (5) blood transfusions Only the last two are at present to be considered applicable to man

In clinical radiation therapy amelioration or reduction in the incidence of nausea and vomiting has been claimed for a number of diverse agents *e g* (1) adrenocortical hormones (2) adrenocorticotrophic hormone (3) various vitamin preparations and (4)  $\beta$  mercaptoethylamine All of these are of somewhat dubious value Lacking a specific therapeutic agent or regime treatment has been asymptomatic and supportive Bed rest fluids antibiotics, and transfusions have been used as indicated

**Problem of Partial Body Shielding** Clinical radiation therapy experience and extensive experimental animal research indicate that shielding part of the body is effective in reducing the magnitude of the acute radiation injury and is associated with an accelerated recovery particularly of the bone marrow It is probably this latter fact that accounts for the reduction in mortality The value of such shielding in military situations is difficult to estimate The degree to which this permits an individual to raise head and shoulders above ground level while in a foxhole or be exposed through an aperture in some other shielding and avoid the consequences of radiation injury is not known An additional problem in shielding considerations is the fact that the more desirable types of shielding for neutrons are not the same as for  $\gamma$  rays

**Description of B to Bur** For localized  $\beta$  radiation the best clinical description available is that of the results in the Marshallese In these individuals the minimum time for development of skin lesions was 12 to 15 days The first indication

of the development of a skin lesion was an increase in skin pigment in localized areas. This was followed by scalp desquamation in the central portion of the lesion, leaving an area of pink depigmented skin. Gradually the pink area spread out into the darker pigmented area, with eventual complete healing. In other areas, presumably where the dose to the skin was greater, blisters developed. These opened, leaving a raw, weeping area. This is comparable to a second degree thermal burn. New skin covered these areas in 7 to 10 days and was followed by pigmentation.

Unfortunately, the dose to the skin could not be measured and cannot be calculated or estimated, other than by comparison with the effects of x radiation given in single or multiple doses. Presumably lesions that developed blisters resulted from a dose to the skin, which if the total body skin were involved, would be lethal. However if lethality is comparable to that observed in thermal burns, involvement of less than 100 per cent of the skin would result in lethality. For example an untreated 33 per cent body surface area second degree thermal burn is in the lethal range. Probably similar results would be obtained with  $\beta$  radiation. Except for  $S^{35}$  the surface dose required to produce recognizable epidermal injury for pigs, sheep, rabbits, rats, and mice is from 1 500 to 5 000 rep. For  $S^{35}$  it is 20 000 to 30 000 rep.<sup>2</sup> Higher doses are needed when  $S^{35}$  and other weak  $\beta$  emitters are used as only a small fraction of the  $\beta$  particles will penetrate to the sensitive layer of the skin.

#### LONG TERM (LATE) EFFECTS

**Shortening of Life Span<sup>24</sup>** The long term effects of irradiation can best be considered from the standpoint of reduction in life span. Animal experimental data clearly indicate that one of the consequences of total body x radiation in sufficient quantity is shortening of life span. This reduction in life span is conspicuous in the case of those who develop leukemia, but other tumors also may have their origin in radiation. In many instances, however there is no specific pathologic change attributable to x radiation except for a general pattern of premature aging. For this reason shortening of life span which represents the end result of all the injury produced is probably the most sensitive and satisfactory criterion for determination of the long term hazard.

There are several different mathematical approaches to the study of this problem. These are the adaptation of the Gompertz formulation to radiation, the Sacher and the Blair theories. From the available animal data the life span shortening in young animals for a single acute dose is on the average per cent per 100 r. The relationship between reduction in remaining life span and dose is linear. For older animals, theory predicts

that the percentage reduction of life span increases approximately threefold

What can be said about man? At present there is only one suitable opportunity for observation and that is the experience at Hiroshima and Nagasaki. It is possible but not probable that some data regarding shortening of life span from a sublethal dose of radiation may become available from the continuing study of the Marshallese. However it has been reported that radiologists have an average life span of 52 years (approximately 12 per cent) less than other physicians not exposed to radiation. This reduction is compatible with the extrapolation of the animal results to man and estimates of the exposure of radiologists to radiation. Brues and Sacher<sup>2</sup> have developed two postulates for the extrapolation from species to species. These are

1 For the single acute dose—the percentage reduction in life span is the same

2 For chronic irradiation—to produce the same percentage reduction in remaining life span the dose rate should be  $\lambda$  where

$$\lambda = \frac{\text{life span species 1}}{\text{life span species 2}}$$

Thus for man the dose rate to produce the same percentage decrease in life span should be approximately one eighteenth that observed in the rodent.

There are two features of Blair's theory and method of analysis that require further explanation. The Blair theory predicts that the acute-dose LD<sub>50</sub> decreases with age and that this decrease is linear. This has been tested in only a very limited way and indeed the acute dose LD<sub>50</sub> does decrease with age in rats but the data are not sufficient to determine the rate of decrease of LD<sub>50</sub> with age. Because of certain pulmonary complications observed in older rats extension of this observation to other species may not be warranted. The Gompertz function type of analysis also predicts that the LD<sub>50</sub> should decrease with age since aging and irradiation injury are additive older animals will require less additional injury whatever the source to produce death if the injury produced is comparable to normal aging. For man there is no information available on this aspect.

Cataracts. The dose to produce cataracts in man is not known with any degree of certainty. It probably is relatively low for x-rays in the range of LD<sub>50</sub> and considerably lower for neutrons. Cataracts are a particularly serious potential complication of neutron radiation. The RBE for cataract formation from neutrons is approximately 10 to 20.

**Fertility** This is difficult to evaluate quantitatively. Depending upon the dose, there can be anything from a mild depression of sperm formation up to permanent sterilization. The dose for permanent sterilization is slightly higher than the lethal dose. In males a single sublethal dose results in a decrease in sperm count; this can be considered as relative sterility. Recovery is a slow process taking up to one year. For the female, doses of 125 to 150 r produce amenorrhea, and 170 r produces sterility of 12 to 36 months duration. Parenthetically it is of interest to note that survivors of serious radiation accidents have produced children.

### GENETIC EFFECTS

That radiation results in genetic changes is unquestioned. While much work has been done on the genetic changes induced in lower organisms, particularly the fruit fly, there are few mammalian experimental data and those almost entirely in the mouse. The great uncertainty for man is the relationship between dose and number of mutations produced and their manner of expression. In general it is assumed that radiation induced mutations are deleterious. Genetic changes would be a problem for the survival of mankind if the whole population or a large fraction of the population were to be heavily exposed. Radiation of small groups is more a problem in the concern of the individual for the welfare of his progeny than for the survival of mankind, but cannot be neglected. With the increasing development and use of various radioactive isotopes for nonmedical purposes and the use of reactors for propulsion and power systems, large numbers of people may be exposed to radiation. Thus, the small groups may become considerably larger in the near future.

There are several observations regarding the genetic changes induced by radiation that may be summarized as follows:

- 1 Most if not all radiation induced mutations are deleterious
- 2 There is no recovery from radiation induced genetic changes
- 3 The amount of injury produced is directly proportional to the total dose

From experimental observations in fruit flies and mice it is suggested that a dose of 30 to 80 r to the entire population would double the mutation rate. The consequences of this are difficult to estimate because the manner of expression of many of these genetic changes is not completely understood. In fact it is but little understood. These changes could find expression in terms of various constitutional deficiencies, varying from those that result in a shortening of life span to those involving

the capacity to perform mental tasks. It is entirely possible that doubling the mutation rate could be a serious burden economically and medically. It has been recommended that the average dose for the reproductive period be kept below 10 r above background. For some individuals this may be exceeded but should be limited to a total dose of 100 r of which no more than 50 r should be accumulated before age 30.

### EFFECT OF PROTRACTION AND FRACTIONATION

Both evidence from animal experiments and experience with clinical radiation therapy clearly indicate that protraction of the delivery of the dose for days, weeks or months or fractionation of the dose over similar periods of time results in a smaller biological effect (generally a lower incidence of lethality) than does a single dose of the same magnitude delivered over a period of minutes. This does not include genetic effects.

This implies recovery from the injury produced by radiation. The rate of recovery may be measured by administering a sublethal dose, generally one half LD, and then at various later time intervals determining the additional dose required to produce 50 per cent lethality. Such experiments show that the amount of the second dose to produce 50 per cent lethality increases with time. However, experimental studies show that recovery is not complete; the irreparable component amounts to about 10 to 20 per cent of the injury produced.

In the mouse, the recovery rate is from 10 to 20 per cent/day; in the rat, 7 to 10 per cent/day; in the dog, about 4 to 5 per cent/day; and in the monkey, 14 per cent/day. The recovery rate for man is not known. Studies of the recovery rate for erythema (reddening of the skin) in man indicate much larger recovery rates; however, this is not the recovery rate desired for military medical purposes. Actually, the recovery measured in lethality experiments is not a single physiologic process; it represents the net recovery of all the physiologic processes necessary for the maintenance of life, with each weighted according to its significance in the maintenance of life.

The effective dose is defined in terms of the results of a single acute dose and is best illustrated by an example. If the acute dose to produce 50 per cent lethality within 30 days is 400 r, then the effective dose of any system of fractionation or protraction that produces 50 per cent mortality in 30 days is 400 r, although the physical dose may be much greater.

From the Blair theory, for the particular case that the animals are young, that each dose is administered within a short period of time, and that death occurs in a few weeks,

$$D_{\text{eff}} = \left[ (nf) + (1-f) \frac{(e^{n\beta t_2} - 1)}{(e^{\beta t_2} - 1)} \right] \Delta$$

where  $f$  = fraction of injury, irreparable

$\Delta$  = dose

$n$  = number of doses

$\beta$  = rate of recovery

$t_2$  = interval between doses (days)

For man it is recommended that  $\beta = 0.05 \text{ day}^{-1}$  be used. It also is recommended that a value of  $f$  between 0.10 and 0.20 be used although there is no evidence to support this recommendation. Other relationships have been proposed for calculation of the effective dose but they are not satisfactory.

### INTERNALLY DEPOSITED MATERIALS

**Source** The radioactive isotopes produced in the process of fissioning of uranium and plutonium in an atomic explosion are distributed widely over the entire world by the winds. There is a slow settling of these particles from the atmosphere, the rate of descent being governed by particle size and shape, and the location of the fallout being dependent upon the rate of descent and wind patterns. There are a number of variables involved, none of which is completely understood. A particularly valuable source of information and summary of the current status of the fallout problem is to be found in the hearings of the Joint Committee on Atomic Energy. The quantity of material in the stratosphere and the rate of movement from the stratosphere to the troposphere have been estimated, the latter having an average residence time of approximately 10 years and the former having been estimated as varying from a few per cent to over 50 per cent for a land burst.

**Route of Entry into Man of Fallout Fission Products** There are three routes of entry:

- 1 Inhalation
- 2 Ingestion
- 3 Open wounds

**Inhalation** During the period when radioactive particles are falling out, inhalation is a route of entry into the body. After settling on the ground, these particles can become airborne again and thus available for inhalation. The distribution within the respiratory passage of radioactive particles inhaled is dependent strongly upon particle size. In general:

- a Particles less than  $0.1 \mu$  are inhaled and then exhaled
- b Particles  $0.1 \mu$  to  $3.0 \mu$  reach the lungs and are deposited in the alveoli



c From  $3.0\ \mu$  to  $10\ \mu$  particles reach and deposit themselves upon the walls of the trachea bronchi and bronchioles, then work up to the larynx and ultimately are swallowed

d Above  $10\ \mu$  particles are filtered out in the nose

Rainfall occurring at the time of passage of the atomic cloud has been shown to result in an increase in the urinary cesium<sup>1</sup> and I<sup>131</sup> content of man strongly implicating inhalation as a significant route of entry

*Ingestion* Radioactive materials settling on the ground may be incorporated into or coat the surface of plants that subsequently are eaten by man or by livestock which later are eaten by man. Evaluation of the importance of this route of entry and the hazard involved is complex. Movement of fission products through the soil uptake by plants, use of plants for animal fodder and subsequent ingestion by man all are important and only partially documented factors. The presence and amount of strontium<sup>90</sup> in man is well documented although the details, particularly quantitative of the movement of this Sr through the biosphere are lacking.

The relative significance of these two routes of entry is still to be determined. Water does not appear to be a significant route of entry of fission products into man. However this may not be applicable for local fallout.

*Open wounds* Open wounds do not appear to be a significant route of entry into man except in unusual circumstances.

*Metabolic Fate* The metabolic fate of the fission products is dependent on a number of factors. For each element it is different and for each chemical species of a given element it may be different. For example particles inhaled and reaching the alveoli if they are soluble in body fluids are absorbed reach the blood stream and subsequently are distributed throughout the body in accordance with the manner in which the body treats that particular compound. If insoluble the particles may be concentrated in the lymphatic system of the lung and remain within the lungs and associated lymph nodes for that individual's lifetime constituting local areas of intense radiation. These considerations of particle size and chemistry must be applied to all of the fission products.

Within the gastrointestinal tract similar considerations apply. For materials that are absorbed the distribution in the body varies. For example iodine as iodide is taken up by the thyroid gland and subsequently released to the blood stream as organically bound iodine.

Probably most important is the fact that many of the fission products that reach the blood stream are taken up and retained for long periods of time by bone. Animal experimentation and

the history of radium dial workers indicate that this may lead to serious complications, such as malignant bone tumors, although other less serious pathologic conditions can and do occur. In fact, in animal experiments it can be shown that such bone deposition can lead to shortening of the life span even in the absence of specific pathologic changes in the bone.<sup>29</sup>

**Biological Effects** The quantities of most materials that can gain entry into the body are such that if a material is not a normal metabolite, the quantity present is not sufficient to be toxic merely by virtue of its chemistry; the injury produced is that of irradiation of the tissues. Depending on the tissue involved, the dose, and the dose rate, a wide range of pathologic changes may occur. These will vary from no discernible anatomical change but with subtle physiologic changes for low doses to the production of malignant tumors at higher doses. The latent period for these changes may, as in the case of radium dial workers, be up to 10 to 20 years or more.

**Therapeutic Aspects** The therapeutic problem is largely concerned with a particular class of isotopes, namely those associated with deposition in the bone and commonly called "bone seekers." Unfortunately, therapeutic measures now under investigation principally removal by chemical agents, are not particularly promising.<sup>30</sup> Therapy of the radiation injury produced by internally deposited radioactive isotopes is as unsatisfactory as for external radiation; there is no good means of treatment.

Analysis of the biological properties of the fission products has indicated that the long-lived isotope of strontium,  $\text{Sr}^{90}$ , is the greatest hazard, although it is not the only long-lived isotope that may be hazardous. Project SUNSHINE has reviewed the biological properties of strontium: the world-wide distribution, in particular in food and water, and the present levels of body burden of  $\text{Sr}^{90}$ .<sup>31</sup> The fact is that  $\text{Sr}^{90}$  is now present in human bone and is thought to be derived from food, principally dairy products. At present the quantity of  $\text{Sr}^{90}$  present in man is low compared to estimated toxic levels. The change in bone  $\text{Sr}^{90}$  content with time is partially known, but a good evaluation of the tolerance level is lacking. Recent work implicates an inhalation route of entry as at least partially responsible for the present body burden. While considerable attention has been directed towards  $\text{Sr}^{90}$ , other fission products can and do gain entrance to the body. It is the bone deposition of  $\text{Sr}^{90}$  that gives rise to concern; the majority of the other fission products are either produced in small quantities compared to strontium or are relatively rapidly excreted or have short physical half-lives. In the latter class fall the iodine isotopes. Nevertheless, they contribute to the injury produced and should not be ignored.

## COMBINED INJURIES

Experiments with swine dogs and rats indicate that the lethality of combined nuclear radiation damage and thermal injury is greater than would be expected.<sup>21</sup> These studies have been carried out by determining the mortality produced by thermal injury alone by radiation injury alone and by combined injuries. For example thermal burns and radiation exposures that by themselves would result in no mortality give rise to significant mortality when combined. Also thermal burns or radiation injury at levels that alone result in low mortality may when combined lead to considerably greater mortality than expected. Quantitative translation of this data to man is not possible at this time. Nevertheless it should be anticipated that in man the same findings will occur namely that these effects are not simply additive. It also is probable that similar results will be obtained when radiation is combined with other forms of traumatic injury. A calculation of the magnitude of this effect is not possible and the variety of types of traumatic injury is such that any calculation would be of little value.

## MAXIMUM PERMISSIBLE LEVELS OF RADIATION

As a fundamental premise it must be considered that all radiation is deleterious. However radiation and certain radio isotopes have come to play important roles. For example great strides have been made in medicine since the introduction of the x ray for diagnostic purposes. Radioactive isotopes have proved to be a potent tool in medical research and to have therapeutic value in certain diseases. The industrial uses of x rays and radioactive isotopes are increasing rapidly and finally reactors are being used for the production of power. With all these beneficial uses there comes the hazard involved.

**External Radiation.** Since the introduction of x rays as more data on the late effects of irradiation became available there has been a progressive reduction in what has been considered to be a safe maximum level of exposure. Handbook No 59 National Bureau of Standards reviews the present tolerance levels. In general it is recommended that for continuous total body x or y radiation the maximum permissible exposure be 300 mr/week.

**Internal Radiation.** The maximum allowable concentration of radioactive isotopes in the body is based largely upon the assumption that the dose rate to the critical organ be no greater than 300 mr/week. Because of varying biological properties the critical organs vary with different isotopes. In general bone and bone marrow are the critical organs although not for all isotopes. Handbook No 59 National Bureau of Standards lists values of the maximum permissible amount for a number

of isotopes. Calculation of these quantities is complex, and depends upon the distribution within the body, the radiations emitted, the biological turnover time and for  $\gamma$  emitters an estimate of  $PBE$  or comparison with radium. There are many uncertainties involved, and like the limits set for external radiation, those for internal radiation are being reviewed.

Recently an additional restriction limits the exposure rate for both external radiation and internal emitters to individuals in controlled areas, i.e., those occupationally exposed and in addition limits the dose according to the formula,<sup>3</sup>  $MPD = 5 (N/18)$  rem where  $N$  = age in years and  $MPD$  = maximum permissible accumulated dose.

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# TOXICOLOGY AT THE ARMY AREA LABORATORY

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**A**N ever increasing demand for the identification of toxic substances in biological specimens has become evident in recent years. A review of this subject, together with a discussion of the submission of specimens may serve to answer a number of questions and to clarify some of the problems encountered.

As stated in Army Regulation 40-440 "Toxicologic studies, virus and rickettsial procedures, and studies in connection with medicolegal and epidemiologic problems will be carried out to the extent that trained personnel permits." It therefore becomes the duty of the Army Area Laboratory to carry out toxicologic investigations for all of its submitting agencies which may, on a regional basis, include certain Navy and Air Force facilities.

The term toxicology, as used in this laboratory, means the identification of foreign substances in biological fluids and tissues. No evaluation of the toxicity of these substances is made, such as determination of minimal lethal dose (MLD) or median lethal dose ( $LD_{50}$ ). Instead the problems studied are use of narcotics, coma possibly caused by sedatives (paralitics), and accidental or intentional poisoning by a great variety of agents. It is this laboratory's function to identify and attempt to quantitate such substances.

## SUBMISSION OF SPECIMENS

One of the most basic problems with which we are faced is the submission of specimens.

### Choice of Specimen Quantity and Packaging

There are several excellent references<sup>1-3</sup> concerning the choice of specimen as related to the suspected substance, and each person submitting specimens should familiarize himself with this information. Table 1 is a partial listing of the type of test desired and most desirable specimen to submit, together with the quantity that should be submitted. In autopsy cases, however, one should submit as many different specimens as considered

necessary to determine the causative agent. Along with biological specimens physical evidence such as syringes, tablets, powders, and other objects that might be implicated, should be obtained and submitted.

TABLE 1. *Chemical and physical evidence to be submitted for analysis*

Possible substance	Specimen to be submitted	Quantity
Alcohol	Blood	50 ml, 500 g
Alkaloids	Urine	All available
Antihistamines	Urine	All available
Barbiturates	Blood	50 ml, 10 ml
Heavy metals	Liver	500 g
Acid	Heart	10 g
Liver	Liver	500 g
Murder	Kidney	1 kidney
Inhalant	Lung	1 lung
Vital poison	Bile	500 g

A thumbnail rule as to quantity is: When in doubt, send more. A good practice for the physician performing the autopsy is to obtain as much as deemed feasible and immediately freeze those tissues. Then upon further investigation one can forward those specimens most likely to contain the suspected agent. Recently 0.5 ml of serum was submitted with a request for tests as to barbiturates and narcotics. Obviously the person submitting the request is unfamiliar with the type of analyses involved. From our viewpoint we would prefer an excess of the sample and can always use a larger aliquot. Remember we often are dealing with microgram quantities and an inadequate specimen can result in failure to recover the substance. Although each laboratory may have slightly different requirements, exact information can be obtained from them directly.

Finally, how should these specimens be packaged? Place each organ in a separate clean glass vessel. Measure the amount submitted and note it carefully in the accompanying request. Seal each vessel. Whatever procedure is deemed most efficient should be used remembering that some device should be employed to prevent tampering. A favorite method is the use of sealing wax marked with a distinctive seal.

#### Shipping Medicolegal Cases

In order for the findings of the laboratory to be accepted as evidence, proof must exist that the specimens have been in proper custody. This is commonly referred to as chain of custody or chain of evidence. To meet these requirements every person handling the specimens and packages must sign his name to this effect. The specimens cannot be mailed by regular or

ordinary mail Registered mail, rail or express, or air express are the only methods of shipment. If possible, a hand carried specimen is most satisfactory. Remember, if there is any doubt as to the validity of the "chain of custody," the laboratory findings may be thrown out as evidence.

In an investigation of this type, the toxicologist generally is located at some distance from the originating agency. The specimens arrive with a request for certain determinations. Many times the request reads, "Toxicologic Examination." No other information is submitted to help. Where then, does he start? An integral part of each case is a clinical history or autopsy protocol. Requests should be as specific as possible; the more specific the request, the more efficient the service.

### DETERMINATIONS PERFORMED

#### Alkaloids

Urine appears to be the best specimen to work with. The alkaloids are determined by ultraviolet absorption spectra and paper chromatography. These compounds are tertiary amines and are basic in nature. Advantage is taken of their similarity for extracting them from urine. We have modified several procedures described in the literature.<sup>6-8</sup> Extractions are made from the urine at two different hydrogen ion concentrations (pH values). The extracts are then concentrated and chromatographed at four different pH values. After migration the strips are air dried and sprayed with an indicator reagent. Positive spots are shown as dark areas on an orange pink background.

It has been shown that when a person takes codeine some codeine is demethylated and excreted as morphine.<sup>9</sup> Figure 1 illustrates the recovery of both morphine and codeine from a patient who had taken only codeine. Further, one can distinguish between a person who has taken morphine and one who has taken codeine as only morphine is excreted when morphine is taken. This was demonstrated by having a volunteer take 1/4 grain of morphine and collecting each urine specimen for the following 120 hours. Morphine was detected easily at 48 hours. Heroin per se is not recovered using the above procedure, but further work is being conducted along these lines.

A second procedure used for detection of alkaloids employs ultraviolet absorption spectra. In many cases, the absorption patterns of alkaloids are specific. The spectra are useful in making an initial screening of urine and blood specimens. The unknown is extracted with chloroform at acid, neutral, and basic pH values. The alkaloids are usually found in the basic fraction, whereas a substance such as salicylic acid is found in the acid fraction. The spectra obtained are compared with spectra of known



substances and a tentative identification made. This gives an indication of what must be done in chromatography for alkaloids or specific chemical determinations for other materials.

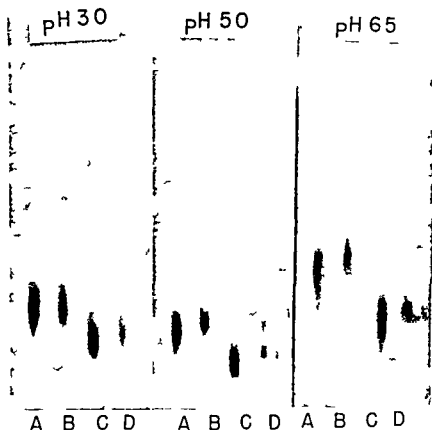


Figure 1 Results of chromatography partition factors. At a given pH the code standard is shown as A the code extract of the sample is shown as B the morphine standard is shown as C and the morphine extract is shown as D. Note how the migration of the bands is similar.

Ultraviolet spectrophotometry also is useful after chromatography. Positive stained areas are cut from the paper and eluted. The paper is treated with reagents to free the substance which then is extracted and examined spectrophotometrically. The ultraviolet spectrum thus obtained is compared to spectra of known substances. The migration data from paper chromatography in conjunction with an ultraviolet spectrum are sufficient to identify almost all of the basic substances of medicolegal interest. Figure 2 shows a comparison of standard strychnine with eluted strychnine. The similarity is excellent proof of identification.

With the use of increasing numbers of pharmacologic agents the picture becomes more confusing. Antihistamines give similar

reactions. We have found that chromatography will easily separate them from the alkaloids, as the antihistamines migrate faster. With the advent of the tranquilizers, however, another problem arose. Several of these substances have properties similar to those of antihistamines and alkaloids, and stain with the indicator. We now are working on this class of agents. An example of the difficulties encountered is the inability to recover Sparine (brand of promazine hydrochloride) from a known urine sample, using the above technique. However, pure Sparine stains with the iodoplatinate indicator and migrates when chromatographed. The

### STRYCHNINE—ULTRAVIOLET ABSORPTION CURVES RECOVERY FROM BLOOD

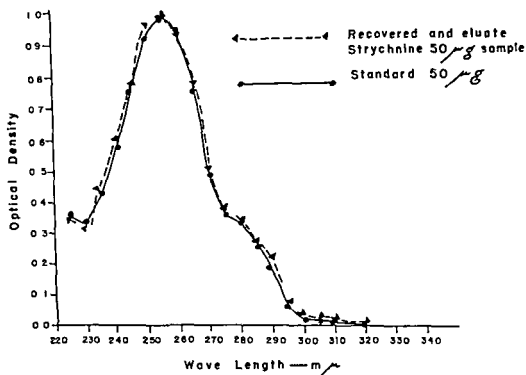


Figure 2 Comparative ultraviolet spectra obtained from a strychnine standard and strychnine recovered from blood. Note the similarity.

problem of the metabolism of these substances is an enigma, and just what the metabolic products will be and how they can be characterized and identified, remains for the future.

#### Barbiturates

The identification of barbiturates has been made simple by Goldbaum's excellent work.<sup>10</sup> Briefly, blood or urine is extracted at two different alkaline pH values and the ultraviolet spectra obtained. A ratio of optical densities at ten different wave lengths is made. These results quantitate the amount of barbiturate pres-

ent and in several cases allow one to determine which class of barbiturate (i. e. short acting or long acting) is present.

### Heavy Metals

This classification includes mercury, bismuth, antimony, arsenic and lead. For the first four a routine screening procedure commonly referred to as Reinsch's test is used. The specimen is hydrolyzed in HCl and a spiral of copper wire is placed in this mixture in an Erlenmeyer flask. This is boiled gently for one hour and the metal, if present, will be deposited on the copper wire. A silver coating indicates mercury, whereas a dark coat indicates antimony, arsenic or bismuth.

Antimony and arsenic can be separated by performing Gutzeit's test. An organically digested specimen is treated with potassium iodide and stannous chloride in a specially constructed generator bottle. Zinc is added and the gas evolved is passed over a paper sensitized with mercuric bromide. The paper will show a stain if positive and this stain can be treated further for identification. The use of known controls as standards gives an estimate of the quantity present.

Quantitative determinations of lead in urine are made routinely by a procedure based on the dithizone reaction.<sup>1</sup> Examination for other metals is by organic destruction with acid followed by hydrogen sulfide precipitation. The precipitate is then analyzed by classical qualitative schemes.<sup>1</sup>

### Volatile Poisons

This group includes many substances such as alcohol (ethyl and methyl) aldehydes, ketones, cyanide, phenols, carbon monoxide and halo substituted hydrocarbons. Recently we have been using the Conway cell microdiffusion procedure for initial screening. This involves the placing of the sample in the outer compartment of the Conway cell, adding liberating agent and trapping the liberated substance in the inner compartment by use of another reagent. The advantages are obvious: ease of sample preparation, use of small quantities and rapidity of determination. Any positive reaction is investigated further by steam distillation and specific chemical test of the distillate.

One exception to the above groups is carbon monoxide. If a determination of this substance is requested, it is quantitated by a procedure based on the difference of spectra of carboxyhemoglobin and reduced hemoglobin.

### Other Substances

A large number of other compounds including amphetamine, bromides, organic phosphorous compounds, fluorides and marijuana have toxicologic significance. If a specific request is

made, an appropriate chemical procedure is employed in performing the test. We are for example able to screen amphetamine by its ultraviolet spectrum. This is then followed by a specific test for amphetamine.

### REPORTS

The rapid reporting of results is of primary concern. This can be greatly expedited by making specific requests. The formal report rendered to the requesting physician gives the results of our findings in detail, but with no attempt at interpreting these results. It would be foolhardy if we were to attempt to determine the cause of death. The addict to arsenic for example, would excrete huge amounts of this metal—amounts that would seem to us to be the cause of death. The requesting physician is in a better position to interpret our findings and there are available several texts in which toxicity of substances is reported.

Many substances never are identified because of improper specimens. They may be inadequate in amount or obtained with too great a time lag (e.g. those from narcotic users). Although several cases are on record with no specific cause of death, I am confident that if a foreign substance is present in adequate quantity, it will be detected. If there is an indication of substances other than those specifically requested, the toxicologist will pursue their identification. Several such cases are in our records. The toxicologist however is not an alchemist—there are no secret procedures for identifying toxic substances. He is a good analytical chemist and is just as concerned with solving the problem as is the person requesting it. The more help the requesting physician can render, the more accurate will be the results.

### FUTURE PROSPECTS

Where will toxicology progress in the future? It is hoped that rapid accurate screening procedures may become available. The advantage of such tests is self explanatory. It also is hoped that these screening procedures can be followed by specific chemical tests which will effectively quantitate the compound. The more investigation done along the line of metabolism, excretion patterns, and identification, the sooner will be the solution of the many problems posed to the toxicologist. Forensic toxicology is no longer in the dark, but it still is standing in the shade.

### SUMMARY

Proper submission of specimens cannot be overstressed, and they should be accompanied by a clinical history or autopsy protocol and a specific request. If there are medicolegal aspects to the case, clinical and toxicological aspects must be maintained. The toxicologist can solve many problems if care is taken to meet the requirements.

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## HOW TO DRIVE TO THE AIRFIELD—SAFELY

Most people are agreed that the average motorist has more dangers and decisions to face than the airline pilot (given relative competence in the respective fields). Pilots have told me that they are safer in their planes than when driving to the airfield. This is borne out by mortality statistics for motorcar travel and scheduled airline travel. Thus the only sensible and practical rule for driving motorcars is: No alcohol for twelve hours before driving or at least to keep the blood alcohol below 0.03 per cent.

—HORACE F CAMPBELL M D

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# SUBMARINE MEDICINE ON U S S NAUTILUS AND U S S SEAWOLF

JOHN H EBERSOLE *Lieutenant Commander MC USN*

**I**N THE past few years the highly specialized field of submarine medicine and submarine physiology has been deeply involved in the revolutionary changes brought about by the advent of the nuclear submarines, "Nautilus" and "Seawolf". To day there is more than promise that the problems of nuclear power will involve all fields of military medicine and this is not limited to military medicine alone for the application of nuclear energy for civilian power already in being in the United Kingdom, promises to bring these problems to civilian medical practitioners, particularly in the field of industrial medicine. While some of the problems met on "Nautilus" and "Seawolf" are limited to submarines because of their unique operational environment, many others apply equally to all reactor installations, either military or civilian sea going or shore based. The experiences that submarine medicine has had in these initial years may, therefore, be justifiably utilized for a realization of the part that medicine will play in the nuclear age.

There are three important areas in which nuclear propulsion has strikingly added scope and depth to the field of submarine medicine. The first of these is a result of the new environmental situation created by reactor propulsion—an environment which has little similarity to that of the conventional submarine. While not so terrible, it is erroneous to think of the medical problems of nuclear submarines as being a simple continuation of previous submarine problems to which has been added the factor of nuclear radiation. The environment of the true submarine, its effects and its control under prolonged submergence, represent a new and unique entity and radiation is but one of its factors.

The second significant change in submarine medical practice is that a nuclear submarine has in the recent past required a radiation control measure during its operational period. For the first time medical and toxicological problems of radiation

submarines have been minimal during in port periods of maintenance. In contrast in nuclear submarines radiation control measures have actually greater significance during *uel* periods than while at sea. It is during this time that reactor shield integrity may be broken in order to allow workmen access to the reactor system and to allow work on contaminated component in areas of radiation flux. Medical personnel must therefore be on the *gui* rce during any such period until the operation is completed in order to control exposure and to insure against spread of contamination. In quantitative terms if alertness may be quantitated approximately four times more attention is required based on relative exposure during maintenance as compared to that at sea.

The third and perhaps most important factor that has expanded the boundaries of submarine medicine is that on nuclear submarines a medical officer is directly assigned as a crew member and is on board for all operations. Evaluation of the medical problems therefore no longer depends upon short term on board observations in a guest capacity. The full impact of this intimacy is only beginning to be realized but it can be assured certainly that definition of the manifold problems cannot help but be improved. The rapid breakthrough in nuclear technology and the acceleration of new developments demand such intimacy for optimum results and maximum benefit to the submariner whose health and efficiency are the prime interest of submarine medicine. This opportunity for daily intimate and long term contact with the submarine and its problems may perhaps be ranked as the most important development in submarine medicine since its inception.

While this paper deals primarily with the radiation problem on nuclear submarine it is necessary in introduction to re-emphasize the point that nuclear power represents more than just a radiation problem to submarine medicine. It is basically a study of the effect of a novel environment on the human organism.

### THE SUBMARINE ENVIRONMENT

It has been stated previously that the nuclear submarine environment is unique. It is necessary however to reiterate this point for it profoundly affects radiation control technique and indeed provides a leitmotiv in the formulation of the radiation hygiene programme.

The single most important factor in the environment with which we deal on nuclear submarines is the capability for long submergence independent of the Earth's atmosphere. All previous submarines have been dependent upon air save for relatively short periods rarely exceeding twelve hours at which time

contact with the Earth's atmosphere was re established. Once on the surface fresh air was circulated in the ship to dilute and displace toxic atmospheric elements accumulated in the ship during its submerged period.

Surfacing of the submarine at that time was required to run diesel engines which, in turn, charged the electric storage batteries which propelled the ship when submerged. Operation of such diesel engines is an aerobic process—the combustion of oxygen and a fossil fuel.

The diesel snorkel has not significantly changed this situation for the snorkel tube, carrying air to the submerged submarine for her diesels, also carried fresh air to the ventilation system and to the crew as a secondary effect. Snorkelling must therefore, be considered as a simple variant of full surface operations in which communication with the open atmosphere is maintained although the ship is submerged.

The impact of nuclear power lies in the fact that splitting or fission of the uranium atom to furnish heat for the production of steam is an anaerobic process—indeed for technical reasons oxygen must be excluded from the process. Given this as the basis for a propulsion system rather than oxygen dependent diesels, true submersible capability is achieved.

Visualize such a true submersible as a streamlined capsule operating beneath the ocean's surface. This microcosm, this subminiature world, must maintain an independent atmosphere and an ecology compatible not only with life but with efficient combat life for the personnel contained within it. A most important limiting factor in this ecology is that such an atmospheric volume is contained and finite; therefore little atmospheric dilution of any toxic airborne substance can be expected. We will see later how this relates particularly to the control of airborne radioactive contamination.

In such an environment three basic conditions must be met in order to support life:

- (a) Continuous supply of oxygen to maintain normal atmospheric concentrations
- (b) Continuous removal of normal human metabolic products like carbon dioxide
- (c) Prevention of or provision for removal of any toxic substance released by ship's equipment

As a corollary to these a vigorous and continuing study must be made of atmospheric conditions aboard to detect and quantify new toxic elements. Experience has shown that many of the so-called "new" elements have existed previously in conventional submarines but were either not recognized or were



quite properly disregarded since significant concentration values were not obtained with the limited submergence times of the pre nuclear period.

Many traps await the unwary in trying to forecast presence or degree of importance of a given toxic substance in such a finite environment. An example is that of carbon monoxide the production of which was previously linked chiefly to diesel exhaust fumes. With the passing of diesel propulsion one might expect this problem to be minimized. On the contrary, tolerance concentrations (100 parts per million) have been reached within thirty hours submerged on nuclear submarines. The chief source now is tobacco smoke, a source not previously emphasized yet of extreme importance with longer periods of submergence.

Another example of an apparently harmless product giving rise to trouble in this new environment is the evolution of radioactive radon gas originating from luminescent radium painted markers. It has been standard practice for many years in our submarines to use radium painted markers and dials for emergency illumination. Such radium of course will produce its radioactive daughter gas radon. Gaseous radon diffuses easily from apparently well sealed components and enters the ship's atmosphere. Here it proceeds to decay into a long series of radioactive daughter elements which become associated with dust particles suspended in the air. They are then easily collected by the filtration devices which operate constantly to monitor the air for airborne radioactivity. Figure 1 shows a rather dramatic increase in airborne beta activity with time submerged—a the result of only six small radium painted switch markers being present on the submarine. Note the abrupt increase in air activity after submerging—a factor of more than ten in twenty-four hours. The curve shows the gradual levelling off as equilibrium is approached in about forty-eight hours. At equilibrium levels are about thirty times higher than when surfaced. Apart from possible biological hazard this represents a serious nuisance because radiation monitoring equipment does not distinguish between such increases due to radon and that due to the much more serious condition of a reactor system leak. One could be justifiably quite concerned by such an increase if due to a reactor system leak. It is therefore necessary to initiate an immediate and complicated identification technique whenever such increases occur. The only solution is to remove all radium sources from the ship and indeed from the entire navy supply system to avoid their reappearance on board.

The problems and other like them have been solved for the most part by removal of the offending source by insistence on more rigid leak tightness requirements in systems containing toxic material or by substitution with less toxic materials.

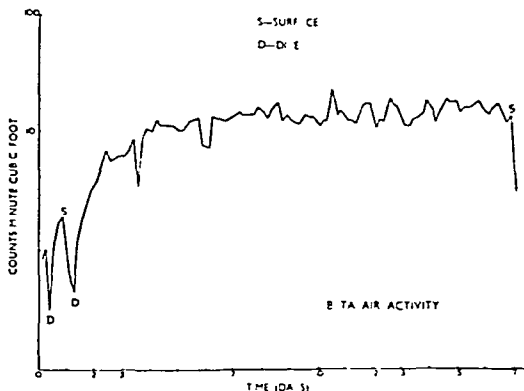


Fig. 1. Radioactivity due to adumbrated markers.

and by development of removal systems such as the  $\text{CO}_2$  scrubber. In the design of removal equipment medical personnel have a vital contribution to make. They must furnish the design engineer with the desired allowable concentration of the toxic substance. In the case of carbon dioxide, for example, it is not feasible to build equipment which will sustain zero concentration; a compromise tolerance concentration must be used. Such tolerance concentrations, however, cannot be based on standard tolerances in the literature which apply usually to the eight hour day, five days per week exposure time of industry. Aboard submerged submarines, where a 24 hours per day exposure is the case, lower tolerance limits must be applied. This principle equally is related to maximum permissible values for radiation levels as well as for toxic gases. It is, thus, one of the prime missions of submarine medicine to establish such limits by investigation and research and to communicate them to the design engineer.

The environmental factors at work here may equally apply to space medicine and indeed in many respects one might simply substitute "space ship" for "submarine" in this discussion.

#### RADIATION IN THE SUBMARINE ENVIRONMENT

Radiation hygiene in a submarine, an environment radically different from that of land based reactors, presents the necessity of adapting and modifying standard control techniques. In many

respects this novel environment is hostile toward efficient radiation hygiene. The following five factors for example will all operate to increase the shipboard radiation control problem.

(1) The closed atmosphere of a submersible allows for little dilution of air borne radioactivity by dispersion in air.

(2) Lack of space for such requirements as decontamination stations and control areas.

(3) Proximity of living eating and food preparation areas to an operating reactor system with an ever present potential contamination hazard.

(4) The submariner's work week which is a seven day week with no possible off site recuperation from exposure.

(5) The constant and relatively rapid re circulation of air through the ship's ventilation system when submerged allows for rapid spread of air borne radioactivity from one spot to another.

If however one examines a submarine more closely there are many inherent factors particularly in its architecture that will tend to assist radiation control. First of all the submarine is arranged horizontally like a long sealed tube. The reactor compartment section of the tube the chief source of radiation can affect personnel only within the compartment itself or immediately forward and aft of it. Shielding is thus simplified and the advantages of locating living areas with zero radiation levels either well forward or aft of the compartment exploited. As far as the crew is concerned shielding in three planes only is vital and full circumferential shielding of the system is not necessary.

An additional important factor is that our sealed tube is horizontally divided into a series of compartments by stout water tight bulkheads. This allows for rapid isolation of a given contaminated compartment simply by shutting a watertight door and securing ventilation to that area. In the case of the reactor compartment ventilation supply and exhaust lines pass through the compartment without openings into it. Since this is the potential area of contamination pick up by the ventilation system can be avoided (fig. 2).



Fig. 2. Submarine compartment layout and ventilation system.

Additional helpful factors are the small number of personnel in a submarine crew which allows for ease of communication and control and lack of multiple exits and entrances that may be guarded by monitoring stations in an industrial plant.

These advantages and disadvantages can be manipulated into an effective shipboard programme. For example, contamination control is built around the compartmentation system and its ease of isolation. Occupancy of the reactor compartment is held to a minimum by placing reactor controls outside this area. Contamination casualty regulations require rapid shutdown of the recirculating ventilation cycle. Protective clothing is dispersed fore and aft of the engineering spaces for accessibility.

Apart from control techniques themselves, consideration of adaptation of radiation equipment is also necessary and laboratory techniques used on board must be modified to meet the peculiar environmental situation of a submarine. Radiocesium calibration sources are prohibited due to the radon problem mentioned previously and cobalt 60 is substituted as a calibration source. Again because of the explosion hazard and high oxygen consumption open flames cannot be tolerated and evaporation of liquid samples must be done by infra-red lamps. Evaporation of large twenty-four hour urine samples as a check on ingested activity is prohibited for health reasons in the confines of a submerged submarine and must wait an in-port period. At sea it would be done only on an emergency basis with an assured lowering of the popularity of medical department personnel among the crew. Volatile solvent in radio-chemical techniques must similarly be avoided. All radiation measuring equipment must be rugged enough for use on board an operating combat ship, a requirement which surprisingly disqualifies many devices used in a shore based installation.

One interesting technique modification is in the use of an end window Geiger Mueller tube for counting of liquid samples. In this a carefully measured 50 ml aliquot of the liquid, usually reactor coolant water, is placed in a standard metal cup. The cup is positioned on a shelf beneath the Geiger tube. Accurate positioning of the cup in relation to the tube is important and is carefully checked with standard spacer and positioning pins. Under these fixed geometrical conditions the number of counts per minute obtained by counting the sample may simply be referred to a predetermined calibration curve of counts per minute versus microcuries per millilitre. If the calibration curve is based on an isotope whose energy approximates that of the sample very accurate results can be obtained to a level of  $1 \times 10^{-7}$  microcuries per millilitre. This is a simple rapid technique and has the advantage of quickly being taught to untrained personnel. It was soon observed that in rough seas

spillage from the cup would result from this procedure. Under such conditions the cup is covered with a thin film of Saran wrap a cellophane type material held firmly in place by a metal lip or rim which fits over the cup. Sensitivity loss when utilizing this is  $10^{-4}$  a reduction to  $1 \times 10^{-4}$  microcuries per millilitre as the lower limit of detection.

These are only a few of the necessary modifications to stand ard techniques and as in the case of radiation control procedures the submarine milieu is all important in determining the degree and type of modification necessary.

### THE REACTOR

Before discussing the personnel exposure problem aboard nuclear submarines it is necessary to describe the reactor system.

A water cooled reactor may be considered simply as a collection of uranium atoms. Bombarded by neutrons the uranium atoms fission or split and release a tremendous amount of radiation and kinetic energy as heat which can be removed by water flowing through the reactor lattice. The two atomic fragments remaining after the parent uranium atom is split are the fission daughters and are intensely radioactive emitting both gamma and beta radiation. These fission daughters cause residual reactor radiation long after the reactor is shut down. The reactor then is responsible both for prompt fission radiation (gamma and neutron) and residual radiation (gamma and beta). They are not the only sources of radiation for the reactor as it operates produces high levels of neutron radiation in its vicinity. These reactor neutrons will activate stable non radioactive atoms present in the coolant water flowing through the reactor lattice.

As water flows through the reactor the temperature of the water is raised by the fission process and this heat in turn is transferred to a steam generation system through a heat exchanger or boiler. The reactor coolant water leaving the heat exchanger is then propelled back through the reactor by a pump. This closed cycle operation of coolant water is illustrated in figure 1. There are two important points to note about this system—first the piping carrying this coolant water is leak proof secondly the steam generated in the heat exchanger is not radioactive. Note that the radioactive coolant water sees the steam only through the walls of the heat exchanger there is no direct contact between radioactive water and the steam. This steam can thus be easily transferred from the reactor area without shielding and can be used to turn a conventional steam turbine.

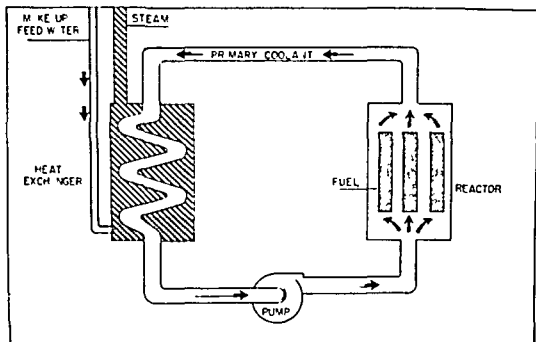


Figure 3 Basic reactor system and coolant cycle

Circulating in the coolant water are the neutron activated radioactive atoms we have mentioned previously. The metallic radioactive atoms will tend to stick on the inner surface of the piping, an important phenomenon having an effect both in raising radiation levels in the area, and in necessitating precautionary measures for contamination control whenever the system piping is opened. These radioactive atoms in the system piping continue to radiate after the reactor is shut down and they are chiefly responsible for the gamma radiation levels in the compartment at that time. The residual fission radiation from the fission daughters in the reactor itself, being well shielded, makes little contribution. In the case of the longer lived radioactive atoms in the coolant water, there will tend to be increasing build up with time so that static conditions will not be met in regard to radiation dose in this area, but will tend to increase.

The compartment containing the reactor system is a section of the submarine termed the reactor compartment. This compartment, essentially a right cylinder, is divided horizontally by a deck forming an upper and lower reactor compartment. The deck is actually a thick shield, below which is placed the reactor and all the coolant system (fig. 1).

Note from figure 4 that the upper reactor compartment has no contaminated coolant water, only non-radioactive steam. Some gamma and neutron radiation will enter the upper level.

through the shield when the reactor is operating but not in any degree which prohibits working in or manning the upper compartment. The highest level of radiation in the upper compartment is above the reactor area and sharply falls off with distance from that point. Levels in the after section of the upper compartment at full power for example are of the order of only 5 mrem per hour

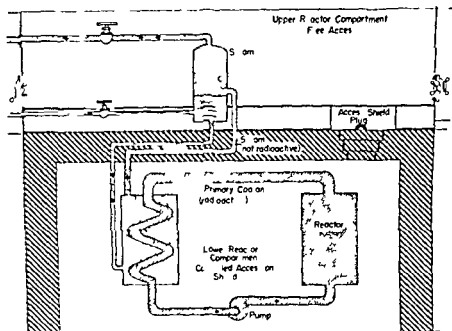


Fig. 4. Reactor compartment layout

It must be emphasized that the reactor compartment is the only area on the ship where a radiation flux exists. All other compartments are similar to those on conventional submarines. Outside of the reactor compartment, crewmen when submerged receive less radiation than when ashore due to the shielding effect of the water on cosmic radiation. This effect is noted on background radiation which decreases to a third of surface value with increases in depth of the submarine.

To return to the lower reactor compartment—the majority of the radioactivity in the coolant water has a short half life and because of its rapid decay the lower area can be entered after reactor shut down. While some reactor residual radiation remains the chief source of radiation is gamma from the plate out activated atoms inside the piping. Normally there will be no exterior contamination present unless the system has been opened previously and contaminated coolant water piled

Prior to entry into the lower reactor compartment after reactor shutdown, ship's personnel are preceded by medical department members who survey and monitor the area checking for surface contamination, air borne radioactivity and degree of potential exposure. Permissible stay times in the lower compartment are determined and requirements for protective clothing, formulated from this information. Monitoring stations are also established at exit points from the compartment and personnel leaving the area carefully checked for contamination. The monitoring points are also used as change areas if protective clothing is required.

### RADIATION EXPOSURE LIMITS—THEIR MEANING

One of the often misunderstood aspects of radiation exposure is a faulty concept of maximum permissible exposure levels particularly in relation to presence or absence of clinical findings. In dealing with any potentially toxic material industrially be it lead, organic solvents or radiation it is necessary for operational purposes to compromise between zero exposure and the levels known to cause detectable biological effects. This compromise value often called tolerance is usually placed well below the threshold of minimum clinical change by a large factor—providing a threshold clinical response is typical of the toxic element in question.

In arriving at such a maximum permissible value one uses historical observations, human clinical data, animal experimentation and laboratory data. For continuous industrial application the permissible exposure arrived at must be well below the threshold known to produce detectable change even if the exposure should last over the entire work life of the individual. This is usually accepted as being thirty years in duration.

Since for many clinical effects the rate of exposure is equally as important as the total integrated amount received over a given period, permissible levels may be expressed in terms of a rate. In the case of radiation the rate of total body exposure rather than the total dose is the more important except for genetic and possibly longevity effects. For example 40 roentgen of total body gamma radiation received over a period of eight years will produce no effect on hematology of the individual yet the same dose if delivered in minutes, will produce demonstrable findings. In this latter case the time dose relationship is such that the rate of tissue regeneration is exceeded by the rate of tissue damage.

The permissible exposure basically used in shipboard shielding design is 300 mrem per week measured in air. Note that this is not a wartime or single emergency, or casualty exposure, but an industrial type application for continuous operation over a work lifetime. If 25 to 40 rem total body radiation is required



by any method which will assure our capability of dealing with the problem.

### DISCUSSION

In reply to a large number of questions by Squadron Leader T. C. D. Whiteside, Air Commodore D. A. Wilson, Dr. B. W. Soole, Rear Admiral G. A. M. Wilson, Dr. D. W. H. Barnes, Mr. D. E. Barnes, Professor G. P. Crowdon, Surgeon Captain C. B. Nicholson, and others, Lieutenant Commander Ebersole said that body odours were overcome largely by the use of the filtration units already installed for removing CO and CO from the atmosphere and by the submarine's ventilation system. The crew also became immune to the residual submarine odour during a long cruise, although others became aware of it when they went ashore. Dispensing with diesel propulsion had not changed this characteristic submarine smell which permeated clothing and was probably contributed to by a number of chemical factors which had not as yet been identified.

He was convinced of the need for the Naval Medical Department to be given full responsibility for the control of the environmental factors including the radiation hazard which were encountered during prolonged submergence in nuclear powered submarines, especially during the developmental period. This allocation of responsibility might not hold, however, for nuclear propelled surface ships. The engineers had their hands full with their own technical problems in submergence and it would be unfair to expect them to give the necessary weight to the human factors which these obviously merited, and they might at times 'rush in where angels fear to tread'. The commanding officer needed the authoritative advice of a medical officer who was technically familiar with the many complex problems involved, particularly as the total situation had not yet been evaluated.

In the United States Navy, submarine medical officers and hospital corpsmen were trained in submarine physiology and plant construction as part of their initial course of instruction before they volunteered for nuclear powered submarines and underwent further training. They had to know the component parts of the engineering plant and even to take part in routine watchkeeping duties. This additional training had paid off time and again during the development stage and early operations of U. S. Submarines *Nautilus* and *Seawolf*.

In reply to Dr. Soole, Lieutenant Commander Ebersole said that saturated caustic soda was used for fission product analysis in place of ammonia hydroxide—a nasty substance to handle in a rolling submarine. Mineral acids were substituted for volatile

organic acids such as glacial acetic acid Pulse height analysis was not used for identifying specific isotopes There were at present difficulties in the use of scintillators which might be overcome

The neutron problem was first tackled by the contractor who was required to shield the reactor to ensure that not more than 10<sup>m</sup> of the radiation dosage was due to neutrons The BF<sub>3</sub> tube instruments for thermal neutron estimation and Radioactive Products Incorporated Model E 1 fast neutron dose rate meter were used as routine monitoring instruments Neutron film badges (Eastman Kodak N T A emulsion of 40 micron thickness) were always worn but they were only developed if the gamma dose exceeded 200 mr in a two week period

Neutron film development was more complex than estimating gamma dosage, as it involved the use of a microscope and oil immersion techniques

In reply to Dr Barnes he showed a picture of the ship's sick bay which was kept quite separate from the radiation laboratory There was, however very little sickness in submarines apart from the customary respiratory epidemics at the beginning of a cruise before the crew became immune to each others strains The number of injuries sustained on the bridge on the surface in conventional submarines was greatly reduced in nuclear powered submarines which spent very much longer periods submerged

In reply to Mr Barnes he pointed out that radiation dosage was not a function of the shield entirely as the greater exposure occurred during maintenance periods when men were beneath the shield Little was to be gained by shaving a small amount of lead off the shield under existing circumstances especially as at a later date the submarine might well be required to carry a large amount of lead ballast when it went to sea a fraction of which could have been incorporated in the shield There would be a gain from reducing the size of the reactor compartment but this would also reduce the accessibility of the component parts within it

### Aviation Group

The aviation group constituted 10.1 per cent of all Navy enlisted males of all periods of service in 1953 and in table 17 it is seen that the control group representation is 20, per cent a close approximation. In the study group and basic study group the proportion is significantly lower suggesting that men serving in this occupation are at lower risk of contracting tuberculosis. An explanation for this is not readily apparent possibly aviation personnel as a total group are not in as close physical contact with their fellows as are ship personnel. Physical standards for the enlisted aviation group are the same as for the Navy enlisted personnel except for a small number (less than 10 per cent) who are directly engaged in flying activities.

### The General Service Group

In 1953 this group comprised 74.7 per cent of all Navy enlisted males of all periods of service while 71.3 per cent of the controls were classified as general service. The proportion in the basic study group is 80, per cent significantly higher than the comparable controls.

The general service group as a whole largely serves on ships with only about 20 per cent not having ship service (table 18). On the other hand it is seen that in the basic study group the proportion having no ship duty is significantly lower in fact 5.8 per cent. Thus it appears that general service personnel with ship duty seem to be especially at risk of tuberculosis.

In seeking an explanation for the apparently higher risk shown for men having ship duty versus those with none table 19 was prepared to compare length of service prior to suspected diagnosis. There is little difference the medians for the two categories in the basic study group general service Navy being 2, and 4 year respectively. Difference in length of service exposure then cannot account for the disparity ship service in itself may therefore be a decisive factor.

An examination of the type of ship served (table 20) reveals that the largest differences occur in the aircraft carrier group possibly indicating a greater risk of tuberculosis for men on these vessels and in amphibious vessels which seemingly afford less. The figures while not statistically significant are in agreement with impression voiced by several senior medical officers of the Navy. Such factors as crowding occupation while on ship duty number of men per vessel and length of time at sea may warrant further investigation.

A more detailed analysis of the general service group divided into its component occupational specialties is shown in table 1. The risk of tuberculosis appears less for the engineering

TABLE 18 *Ship duty in service prior to suspected diagnosis male Navy general service (360) enlisted basic study group*

Category	Cases		Controls	
	Number	Per cent	Number	Per cent
A Ship duty				
Yes	134	91.2	142	79.8
None	13	8.8	36	20.2
Subtotal	147	100.0	178	100.0
Unknown	2		2	
Total	149		180	
B Amount of ship duty				
Less than 50 per cent	30	22.6	34	24.5
50 per cent or more	103	77.4	105	75.5
Subtotal	133	100.0	139	100.0
Unknown	1		3	
Total	134		142	
Median percentage	73		71	

P &lt; 0.05

TABLE 19 *Length of service in military general service basic study group according to percentage of ship duty*

Length of service	Cases				Controls			
	Ship duty		Non ship duty		Ship duty		Non ship duty	
	Number	Percentage	Number	Percentage	Number	Percentage	Number	Percentage
Less than 1 year	3	2.3	1	7.7	9	6.5	12	33.3
1-2 years	33	24.8	2	15.4	36	25.9	11	30.6
2-3 years	61	45.9	8	61.5	57	41.0	9	25.0
3-4 years	30	22.6	2	15.4	37	26.6	3	8.3
4 years or more	6	4.5	0	0.0	0	0.0	1	2.8
Subtotal	133	100.0	13	100.0	139	100.0	36	100.0
Unknown	1		0		3		0	
Total	134		13		142		36	
Median years	2.5		2.4		2.4		1.5	

TABLE 20 Typ f h p rv m l N y g l rv  
l t d b c t dy g p

Typ f h p	C		C l	
	N mb	P t	N mb	P c
A ft c	31	23 1	18	12 7
Cru	13	9 7	12	8 4
D t y	30	22 4	27	19 0
Amph b s	15	11 2	31	21 8
A l	35	26 1	39	27 5
All oth	10	7 4	15	10 5
T tal	134	100 0	142	100 0

B l h p b m n m m d, rv m d p l  
D ff th b g t i g f t

TABLE 21 S rv c p t m l N y g l rv  
l t d b c tudy g p

S rv p t	C		C tr l	
	Numb	P t	N mb	P t
Deck d d	28	18 9	22	15 5
E g g d h ll	27	18 2	47	33 1
Adm i t t and l l	34	23 0	37	26 0
P t t l k	52	35 1	19	13 4
All th	7	4 8	17	11 9
S bt t l	148	100 0	142	100 0
Unk w	1		38	
T l	149		180	

P < 0.001

C tr t p q p m t w d l tr m ll  
D ff th b g t g if  
= 4 x 2 = 25 75

and hull servicemen again for reasons presently unknown. Although the risk among potential strikers appears highly significant, there is some doubt as to the accuracy of occupational classification in this study. As is seen by the relatively large number of unknowns in table 21, information about service occupation was frequently unavailable for the control group and the available data, particularly on the strikers, were less precise in comparison with the study group. Potential strikers are usually

young enlisted men, not long out of "boot camp" who are under training for rated occupational positions or are acting as general duty hands. Their occupational duties are of many varieties and include those of many of the other job categories listed in the table.

Analysis of service occupation and ship duty for the Marines was not rewarding. Almost all (98.3 per cent) men in the Marine Corps were in the so-called "460 Group" which is, broadly speaking, general service. The Marine Corps is primarily a fighting force whose logistical support is largely performed by the Navy. Occupational specialities in the force are relatively few. With minor exceptions, Marines are shore based and the question of Marine Corps ship service is not believed pertinent to the analysis.

The distribution of enlisted grades in the service showed no remarkable difference between the study and control groups.

#### Basic Training Camp

The "boot camp" or basic training center is the place where the Navy or Marine Corps recruit first comes into close contact with thousands of other young men from many parts of the country. This period of training lasts two or three months or longer and presents a favorable opportunity for the spread of upper respiratory disease. While the preinduction medical screening procedures should have all but eliminated the possibility of a recruit with tuberculosis infecting others at camp, there could conceivably be cases among the training cadre which could infect the recruits. To see if this might be the case, table 22 was prepared. The results are negative. The various training camps furnished cases of tuberculosis in about the same proportion as they trained recruits year by year.

#### Marital Status and Mode of Living

These factors were considered in an effort to estimate the time servicemen spent away from the milieu of service life. All men, of course, have off duty periods but married men, particularly in the higher grades, often live with their wives and children and not in barracks. The question has, therefore, certain consistent aspects. Despite the fact that records containing positive information showed that about 22 per cent of the men in both groups were married, less than 6 per cent lived with or visited their families or relatives.

As expected almost all (well over 90 per cent) of both groups lived in barracks or ship. That a slightly but significantly higher proportion in the basic study group lived with their families is not due to better history taking by interns; this information was based on personnel records equally appraisable in both groups.

Although this finding might lead one to suspect that familial contact with tuberculosis might explain the difference it was found that only one of the 13 initially tuberculin negative tuberculous men who frequently visited their families had a history of contact with a known tuberculous family member while in service

TABLE 22 Y f d ct and pl f b t m g f mal enl t d  
bas tudy group by erv

T g		1948	1949	1950	1951	1952	1953	1954	T tal	P
N vy										
G t L k	S	3	5	17	26	11	0	1	63	34.2
	C	0	2	16	53	14	4	0	89	35.2
Sa D g	S	1	4	20	29	25	4	1	84	45.6
	C	1	2	30	34	30	6	1	104	41.1
B bndg	S	0	0	0	8	16	0	0	24	13.0
	C	0	0	1	12	23	6	3	45	17.8
O h	S	0	0	11	2	0	0	0	13	7.1
	C	0	0	4	10	1	0	0	15	5.9
S b t l	S	4	9	48	65	52	4	2	184	100.0
	C	1	4	51	109	68	16	4	253	100.0
Unk wn	S	0	0	1	0	0	0	0	1	
	C	0	0	0	0	0	0	0	0	
T t l	S	4	9	49	65	52	4	2	185	
	C	1	4	51	109	68	16	4	253	
Mar										
S D g	S	1	0	3	3	10	4	0	21	45.6
	C	0	1	4	0	15	10	2	32	41.0
P I l d	S	0	0	3	7	9	5	1	25	54.4
	C	0	2	8	16	12	6	1	45	57.7
Oth	S	0	0	0	0	0	0	0	0	0.0
	C	0	0	0	0	1	0	0	1	1.3
Sub t l	S	1	0	6	10	19	9	1	46	100.0
	C	0	3	12	16	28	16	3	78	100.0
T l	S	1	0	6	10	19	9	1	46	
	C	0	3	12	16	28	16	3	78	
G d l	S	5	9	55	75	71	13	3	231	
	C	1	7	63	125	96	32	7	331	
P by y	S	22	39	238	325	307	56	13	1000	
	C	03	21	190	378	290	97	21	1000	

S = B st dy g p  
C = C mp bl l g p

### Foreign Service

During the years covered by this study, most service personnel on foreign duty were either in the southeast Asia area or in the Atlantic, Caribbean, and Mediterranean areas. The data were examined to see if foreign duty, which presumably in some areas involved contact with people in whom the incidence of tuberculosis was higher than in the United States, exerted an effect. Tables 23 to 27 present the findings in this respect. As was the case in considering ship duty, it is the general service group of Navy enlisted men, and also Marines, who are of chief interest here.

TABLE 23 *Foreign service experience of male enlisted basic study group*

Category	Cases		Controls	
	Number	Per cent	Number	Per cent
Foreign service	171	81.8	170	62.7
No foreign service	38	18.2	101	37.3
Subtotal	209	100.0	271	100.0
Unknown	22		60	
Total	231		331	

P < 0.001

Table 24 shows the distribution of the cases and controls according to the total number of years of service and whether or not the men had had foreign service. For both groups, the percentage with a record of foreign service increases with length of service. Except in the case of men with less than one year of service where the numbers are quite small, a larger percentage of the study group than of the controls had had foreign service. In order to remove the effect of service, the percentages of men who have had foreign service were adjusted to a standard population, the combined number of study and control men with each specified period of total service. Adjusted percentages are 77.6 and 65.1 for the study and control groups respectively. It therefore appears that foreign service had an influence on the development of tuberculosis in men who were uninfected upon entry into the service although the number of controls for whom this item was unknown is disturbingly large.

The time from last satisfactory x-ray examination to suspect diagnosis was examined and found to differ but little between



men who had had and those who had not had foreign service the medians being 15.0 and 13.6 months respectively. Navy and Marine personnel had generally similar distributions.

Navy case finding activities for men serving overseas seem to compare reasonably well with programs for men serving only in the continental United States. This is further substantiated by the fact that the extent and activity of tuberculosis was about the same in the two groups at the time of diagnosis.

TABLE 24 Foreign service personnel according to length of time since last active service group

Length of service (months)	Continental			Overseas		
	Total Number	Whitely		Total Number	Whitely	
		Number	Percent		Number	Percent
0-12	13	1	7.7	43	6	14.0
12-24	58	45	77.6	73	44	60.3
24-36	90	79	87.8	93	68	73.1
36-48	38	37	97.4	57	48	84.2
48 and over	10	9	90.0	5	4	80.0
Total	209	171	81.8	271	170	62.7

Adjusted with foreign service 77.6 65.1  
 Difference between foreign service groups 12.5  
 Standard deviation of difference 3.4  
 Probability of difference being due to chance 0.001  
 Adjusted for difference in foreign service 77.6 65.1  
 Difference between foreign service groups 12.5  
 Standard deviation of difference 3.4  
 Probability of difference being due to chance 0.001

Whether foreign service was mainly aboard ship or on a shore base seems to have no influence in respect to disease among enlisted Navy men although one might suppose that shore-based sailors would have more contact with civilians.

The areas of foreign service were studied in some detail. There was difficulty in deriving exact places from the records and frequently notations of multiple areas of foreign service were troublesome in compilation. Because of the small numbers involved it was found impractical to be very specific in analyzing geographic areas. Consequently the data were consolidated in table 25. These data indicate that the risk of infection is significantly higher in the Japan area and Mediterranean areas for Navy personnel. Inasmuch as essentially all Marines with foreign service were assigned to the Pacific and most of these to I area no statement can be made regarding their relative risks.

TABLE 25 A *Time to return for re-examination of basic study group by sex*

A	Navy				Mar Corps			
	C		Controls		C		Controls	
	Numb	P	Numb	P	Numb	P	Numb	P
Pf (na A both)	83	61.0	79	6.2	33	94.3	40	93.0
Al	(6)	(45.6)	(3)	(5.2)	(30)	(85.7)	(33)	(87)
Carbb	7	5.1	11	8.7	1	9	0	0.0
Med re	9	6.6	18	14.2	1	2.9	3	7.0
Oth and mb	23	16.9	9	1	0	0.0	0	0.0
na on f ho	14	10.3	10	7.9	0	0.0	0	0.0
Sub or l	136	100.0	127	100.0	35	100.0	43	100.0
N f gm rv	27		(9)		11		3	
Unk wn	2		57		0		3	
Tot l	185		53		46		8	

B d l d f e d a s l a d l a n d a r o u h g o n h  
P-CO 001 2 29 99 5

The difference between foreign areas did not seem to be due to differences in total length of service or length of time spent outside the United States.

In the basic study group the time from the start of the longest period of foreign service to the date of suspect diagnosis was determined as well as the duration of the longest period of foreign service (table 26). The medians of these two variables for the Navy enlisted basic study group are 19 and 15 months, respectively, and for Marines they were 14 and 13 months, respectively. The median duration of longest foreign service for the service categories of the comparable controls (tuberculin negative) was 16 months for the Navy and 12 months for the Marine Corps thus, in this regard, there was no appreciable difference in length of foreign service between the basic study group and its comparable controls.

The finding in the basic study group that Marine Corps cases were brought to suspect diagnosis faster (by 5 months) than Navy men, after beginning foreign service, warranted investigation. It appeared possible that the Marines may have had a more severe infection and were more frequently discovered because of symptoms. While this seems to be the case, at least in relation to symptoms (table 27), nevertheless, again, the numbers are too small for adequate analysis.

Marines spent less time overseas than Navy men, and although it might be suspected that they had the benefit of earlier x-ray screening on return to the United States, it has already been

TABLE 26 Duration of long overseas service for men and women in the study

Month	Navy				Marine Corps			
	Count		Percentage		Count		Percentage	
	Number	Percent	Number	Percent	Number	Percent	Number	Percent
Less than 6 months	12	17.6	4	7.3	4	12.9	9	29.0
6-12 months	16	23.6	15	27.3	8	25.8	7	22.6
12-18 months	13	19.2	12	21.8	19	61.3	13	41.9
18-24 months	14	20.6	12	21.8	0	0.0	2	6.4
24-36 months	11	16.2	10	18.2	0	0.0	0	0.0
36 months or more	2	2.8	2	3.6	0	0.0	0	0.0
Subtotal	68	100.0	55	100.0	31	100.0	31	100.0
Not in service	7		69		11		32	
Unknown	90		129		4		15	
Total	185		253		46		78	
Median months	15		16		13		12	

Included were those who were overseas and those who were not included were those who were not included

noted that the overseas annual chest x ray program compared well with that in the continental United States. Further, as shown in table 27, only 29 per cent of the Marines with foreign service were brought to diagnosis by routine annual x ray.

Further analysis of reasons leading to a suspicion of tuberculosis and of the stage of the disease at diagnosis for larger groups in this study is presented in a later section.

### Combat

During the period 1950-1953 many Marines were engaged in ground combat in Korea. The question as to whether the privations of combat affected the incidence of tuberculosis in this group was of interest. Definite information as to participation in combat was elusive in the medical records. Among those for whom it was known there was no significant difference between the study and control groups.

Only one or two of the Marines in the study were noted to have been wounded in action.

### Prisoners of War

Throughout the literature on tuberculosis in the military, frequent mention is made of its high incidence among prisoners of war. Of the approximately 800 Navy and Marine Corps men missing in action in the Korean War, only 184 (157 Marines, 27 Navy)

TABLE 1. *Physical examination of prisoners of war in the Far East, 1945-1954*

C d g	C l f t l d g n o									
	P l m o r y t b e l t e						O r t h e c l		T l	
	N		P e c t		N		P e c t		N	
	N	P e c t	N	P e c t	N	P e c t	N	P e c t	N	P e c t
Phy l y m p t i c m d g n	0	0.0	11	37.9	9	31.0	9	31.0	29	4.0
R u n n e a n n u a l	9	30.0	15	50.0	4	13.3	2	6.7	30	43.5
All h	3	33.3	6	66.6	0	0.0	0	0.0	9	14.5
T t l	12	1.6	3	47.1	13	19.1	11	16.2	68	100.0
Mar Phy l y m p t i c m d g n	0	0.0	6	33.3	6	33.3	6	33.3	18	58.1
R u n n e a n n u a l	5	55.5	3	33.3	1	11.1	0	0.0	9	29.0
All h	1	25.0	2	50.0	0	0.0	1	5.0	4	13.0
T t l	6	19.4	11	35.5	7	22.6	7	2.6	31	100.0

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were repatriated in the large prisoner exchange of August-September, 1953. Only one of this number, a Marine Corps private, was found to have incurred tuberculosis while in captivity, based on findings of the physical examinations of U S prisoners performed immediately after repatriation. No other former POW's were noted in this study, as having developed the disease in service up to 31 December 1954, the terminal date for the study. It is not known, of course, how many men developed tuberculosis and died while in the hands of the enemy or how many developed the disease after leaving the service following repatriation; the latter figure would require a search of Veterans Administration files and was not attempted in connection with this study.

## OTHER CHARACTERISTICS OF THE STUDY GROUP

### Time from Suspect Diagnosis to Final Diagnosis

The remainder of this report is devoted to a further consideration of the tuberculosis case series selected for study, with a view to learning their clinical character and evaluating as far as possible the adequacy of case finding methods employed.

The time elapsing from suspect diagnosis to final diagnosis was studied in terms of the median number of months required

by the Navy Medical Department to study male enlisted cases of tuberculosis and make the final diagnosis. This might be important in relation to changes in extent of disease occurring during clinical study. The median for the male enlisted study group falls under one month. 81.5 per cent of the cases were given a final diagnosis by the end of the third month. It is therefore considered that the classification of the disease at final diagnosis may be used as essentially synonymous with stage at discovery.

In seven cases 12 or more months elapsed between suspect and final diagnosis. These were mostly men who had a suspicious routine film recorded while at sea or on the move and through administrative delays were not admitted to a hospital until much later.

#### Reasons for Suspecting Tuberculosis and Classification of Disease at Final Diagnosis

The event bringing the tuberculous individual to medical attention is important in tuberculosis control. The study results confirm the value of routine annual chest x ray programs in the Navy and Marine Corps.

The routine annual chest x ray was responsible for the discovery of 35.6 per cent of the entire enlisted study group (table 28). It is disappointing, however, that an even larger number (46.0 per cent) were discovered as a result of symptoms or signs of the disease. The finding that only 9 per cent were picked up on discharge examination is remarkable if there had been no annual chest x ray program the figure would undoubtedly be much higher.

Minimal tuberculosis was largely discovered by routine x ray (60.8 per cent) and far advanced disease by symptoms or signs (73.9 per cent). Moderately advanced disease was detected about equally through x ray (41.7 per cent) and by symptoms (36.4 per cent). Notable also was that all other tuberculosis was mainly disclosed following symptoms (82.3 per cent). About 50 per cent of this category is made up of tuberculous pleurisy (BDN 0041, 0042). The 220 cases of moderately and far advanced active pulmonary tuberculosis together here represent 55.5 per cent of all tuberculosis and the 79 cases of minimal active disease 19.9 per cent. Tuberculous pleurisy accounts for about 9 per cent of the total.

There was no distinct difference in the stage of disease at final diagnosis depending on whether the individual was tuberculin positive or negative (table 29) and it does not appear that those who reacted strongly developed relatively more severe forms of the disease than did those with weaker reactions. However, all other types (chiefly pleurisy with effusion) were

relatively more frequent among those who were tuberculin negative or, at least, doubtful reactors. This is consistent with the view that tuberculous pleurisy as the first manifestation of the disease generally occurs soon after infection.

TABLE 28. Clinical course of patients at final diagnosis

Clinical course	Primary infection								Observed		Total	
	Males				Females							
	N	Per cent	N	Per cent	N	Per cent	N	Per cent	N	Per cent	N	Per cent
Physical symptoms	11	11.9	55	36.4	51	3.9	0	0.0	65	8.3	1	46.0
Read reaction	4	60.8	65	41	14	0.3	11	61.0	5	6.3	141	35.6
Dish	15	16.4	14	9.5	1	1.4	5	16.6	4	5.0	55	8.8
Urinary findings	2	2.5	11	7.3	1	1.4	1	5.6	3	3.8	18	4.5
Specimen examination	3	3.8	4	2.6	1	1.4	1	5.6	0	0.0	9	2.3
Re-examination	2	2.5	2	1.3	1	1.4	1	5.6	1	1.3	7	1.8
Observed	0	0.0	2	1.3	0	0.0	1	5.6	1	1.3	4	1.0
Total	79	100.0	151	100.0	69	100.0	1	100.0	79	100.0	39	100.0

In all 100% of cases observed at final diagnosis

### Demonstration of the Organism and Tuberculin Sensitivity at Final Diagnosis

Tuberculin sensitivity on entry into service apparently was not a significant factor in demonstration of the organism at diagnosis (table 1).

Only about 81 per cent of all cases in the study group tested with PPD (first strength) and read reacted positively at final diagnosis (table 30). However at least 54 (83 per cent) of the nonreactors to this dose were positive when injected with PPD (second strength). Seven (2.5 per cent) of 267 enlisted males from whom *Mycobacterium tuberculosis* was recovered did not react to either strength PPD. The total sensitivity, both strengths considered, was in the order of 97 per cent for the entire group, and this was true of the organism positive cases considered separately.

### Sensitivity to Coccidioidin and Histoplasmin at Final Diagnosis

For some years the Medical Department of the Navy has routinely used in major hospitals the coccidioidin and histoplasmin tests in examining all patients suspected of having tuberculosis. Recently in several of the training centers these tests also have been given to recruits and reactions entered on the individual immunization register.

The status of sensitivity to these tests in the study group is shown in table 31. Contrary to expectation there was less sensi-

TABLE 29 Cl / t / t b l / t f l d s l / t l l p / t t r y t m  
by t b l t dy gro p

Cl f	N g t		1 pl d b f l		2 pl		3 4 pl		T l P d u b f l		U k w		T t l	
	N	P t	N	P	N	P	N	P	N	P	N	P t	N	P t
A t P l m a r y	46	19 5	7	18 9	6	22 2	8	26 7	21	22 3	17	22 7	84	20 8
M m l	89	37 7	16	43 2	10	37 0	13	43 3	39	41 5	24	32 0	152	37 5
V d t l y d a n d	42	17 8	7	18 9	5	18 5	3	10 0	15	15 9	12	16 0	69	17 0
F d d	8	3 4	0		1	3 7	3	10 0	4	4 3	6	8 0	18	4 4
I P l m r y	51	21 6	7	18 9	5	18 5	3	10 0	15	16 0	16	21 3	82	20 3
All h														
T t l	236	100 0	37	100 0	27	100 0	30	100 0	94	100 0	75	100 0	405	100 0

TABLE 30 The results of the first and second readings of the PPD test

Category	By the first reading		By the second reading		Total	
	Number	Percentage	Number	Percentage	Number	Percentage
PPD 1st reading (0.00005 ml)						
Positive	4	84.6	4	76.9	8	81.3
Doubtful	1	19.2	0	0.0	1	11.1
Negative	3	13.8	29	53.1	32	100.0
Total	4	100.0	10	100.0	36	100.0
PPD 2nd reading (0.0005 ml)						
Positive	30	81.1	4	85.7	34	83.1
Doubtful	7	19.9	4	14.3	11	16.9
Negative	1	2.8	8	100.0	9	100.0
Total	38	100.0	16	100.0	54	100.0
Total positive	34	92.1	28	100.0	358	90.0

1 more to PPD 1st reading

TABLE 31 The results of the first and second readings of the PPD test, plus the results of the third reading

Category	By the first reading		By the second reading		By the third reading		Total	
	Number	Percentage	Number	Percentage	Number	Percentage	Number	Percentage
Cocci	35	13.6	13	15.7	0	0.0	48	13.8
Doubtful	1	0.4	0	0.0	0	0.0	1	0.3
Negative	86	86.0	0	84.3	7	100.0	93	85.9
Subtotal	258	100.0	83	100.0	7	100.0	348	100.0
Unknown	31		16		1		48	
Total	289		99		8		396	
Fluoropl	64	24.7	15	18.1	2	28.6	81	23.2
Negative	195	53.3	68	81.9	5	71.4	268	76.8
Subtotal	59	100.0	83	100.0	7	100.0	349	100.0
Unknown	30		16		1		47	
Total	289		99		8		396	

tivity to histoplasmin in the organism negative group than among those from whom *Mycobacterium tuberculosis* was recovered. The difference is not statistically significant, but at least suggests that histoplasmosis was not erroneously diagnosed as tuberculosis with any appreciable frequency.



## DISCUSSION

Several of the positive findings of this study are confirmatory of the work of others. Palmer, Jablon, and Edwards have demonstrated the difference in relative incidence of tuberculous disease in previously infected and uninfected men. The question of whether reactors or nonreactors are at greater risk of tuberculous disease has long been discussed. Studies of nursing students as summarized by Daniels generally have indicated that nonreactors were more vulnerable; this also has been true among inmates of institutions where the infection risk is high. In other groups where the risk is not so high, the nonreactors have fared better as in this study. One explanation for this apparent paradox, as suggested by Zacks and Sartwell, is that in the community the reactor frequently is a person with heavier risks of re-exposure to *Mycobacterium tuberculosis* in past and current environment than are found in the environment of the nonreactor; also there is the opportunity for endogenous development of disease in the reactor. The nonreactor placed in a situation where risk of infection is high, on the other hand, has to endure the extra hazard of disease which accompanies the first few months after infection and which the reactor has already passed.

Inasmuch as the environment of reactors and nonreactors in military service is similar, we may conclude that it is the endogenous spread of *Mycobacterium tuberculosis* from their inapparent foci that is responsible for this greater incidence of tuberculosis in reactors. While the risk of reactors in this situation is greater than that of nonreactors, it must not be forgotten that the actual number of cases among the initial nonreactors in this study constituted over 70 per cent of the total, in consequence of the high proportion of men who were uninfected at entry (over 90 per cent).

The findings with respect to the constitutional factors of height and weight are confirmatory for at least three earlier studies as previously mentioned. The influence of foreign service, ship duty, and naval occupation has not, it is believed, been previously demonstrated.

The study suggests that the methods employed by the Medical Department of the Navy to control tuberculosis are useful and reasonably efficiently performed. It is believed that the use of the annual chest x-ray on all personnel has brought about the early discovery of a large number of cases of tuberculosis that otherwise would only have been picked up at re-enlistment or discharge. This is shown by the fact that 35.6 per cent of all cases in the study group were revealed by the routine annual chest x-ray and only 10.6 per cent through re-enlistment and discharge examinations.

## SUMMARY AND CONCLUSIONS

A study has been made of cases of tuberculosis diagnosed in a two year period (1953-1954) in the U. S. Navy and Marine Corps among personnel with less than six years of military service. The primary purpose of this study was to determine epidemiologic factors of importance in the occurrence of tuberculosis in a military service. A secondary purpose was to evaluate the tuberculosis control measures that were employed. As controls for this study, a sample of all cases of acute appendicitis, occurring in these services during the same time period and matched with the study cases of tuberculosis for length of service, was utilized. The most striking differences between the tuberculosis cases and the controls were as follows:

1. A much higher proportion of the tuberculosis cases than of the controls were tuberculin positive on first entry into service. The incidence of tuberculosis is estimated to have been 3.6 times greater in reactors to tuberculin than nonreactors. The frequency of nondisqualifying pulmonary lesions identified on routine roentgenogram at entry was higher among tuberculin positives of the study group of tuberculosis cases than among the nonreactors.

2. The proportion of nonwhite persons was higher in the study group of tuberculosis cases.

3. Comparison of the height and weight distribution revealed an excess of tall men and of underweight men in the tuberculosis group.

4. Occupational analysis revealed an excess of tuberculosis in the general service group of the Navy, particularly in the category known as "potential strikers" and also within this group in men who had ship duty.

5. There was a marked excess of Navy personnel having had foreign service, particularly in the Japan, Korea and Mediterranean areas, in the tuberculosis group.

6. Analysis of data relevant to effectiveness of Navy case finding procedures, such as the interval from last negative film to development of tuberculosis, the stage of the disease, and symptomatic status, indicates that procedures for early diagnosis are reasonably satisfactory.

7. This study has again demonstrated the importance of constitutional factors, of factors related to prior infection with *Mycobacterium tuberculosis*, and of factors concerned with the military environment in the epidemiology of tuberculosis in the Armed Forces.

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## IS DIPHTHERIA CONTROL IN DANGER

It i di tinctly possible that our excellent record of diphtheria control is in jeopardy b c use in many communities the proportion of immune ndividuals has f llen f t bel w 70 per cent We f ce the interesting paradox of having produced a ped min tly us eptible p pul t on as a e ult f immunization prog ms Wh n dphth ia was rampant as h gh a prop rtion of the adult population as 90 p r c nt had acquired a n tural immunity The tural booster effect of a large re e v r f infect o maintained th s l vel of m m nity T day a gre t many children re m m nized n nfa cy Th s m m nity often is not m nta ned either th ough t ost r inject on or thr ough natu al exposure fiv ye rs after p m ary immunization one third of the pe ons n t h g ce ved booster injections ag n are us ceptible to d phthe a s ndic ted by th Sch ck test Persons who never h e b en artif ci lly m m nized r frequently sus ceptible throu ho t thei ad lt l fe bec use of the decreased opp rt nity to cquire nat r l m m nity The consequence of th s might be pr d cted Alth ough adult cas s ha e dropp d fo rfold f om the p v ous decades to th past de de de th hav decrea ed but lightly and an om nous rise in dult fatality s noted For higher ge groups case fat l t es beg n to d c e se but h ve tak n a sharp se n th l st dec d Late ye rs hav shown a con p i ou n mb r of d phther a ca es n old p ople

—C ARDEN MILLER M D  
P t g d t M d c  
p 447 448 N 1957



From December 1952 until 22 March 1953 the patient was hospitalized continuously in a civilian hospital. No records are available from that hospitalization but apparently the patient had a refractory anemia which required repeated blood transfusions.

On 27 March 1953 the patient was transferred to the U S Naval Hospital Memphis Tenn and while there continued progressively downhill with frequent nausea and vomiting. The blood urea nitrogen rose from 56.4 mg per 100 ml on admission to 109 mg per 100 ml on 21 April. Chlorides varied between 125 and 150 mEq per liter. The patient received daily infusions of 10 per cent dextrose in water and numerous blood transfusions. No sodium chloride was given. She was digitalized shortly after admission but this was discontinued after several days. Phenobarbital was given to control restlessness and convulsions. Blood pressure was recorded at 160/115 mm Hg on occasions. The patient was reported to have had episodes of pulmonary edema and hypertensive crises with convulsions. She was transferred to the Walter Reed Army Hospital on 3 May 1953. For several days prior to her transfer she had frequent epistaxes and regurgitation of blood from the stomach.

**Physic I Examination** Admission examination revealed a well developed edematous semicomatose white woman who responded only to painful stimuli by crying. Her blood pressure was 120/60 mm Hg pulse 68 per minute temperature 97 F. Head and neck. There was no nuchal rigidity the thyroid was not enlarged and there was no venous distention in the neck. The pupils were dilated and reacted sluggishly to light. Fundusoscopic examination was negative. There was crusted blood in both nares. Chest examination was negative. The heart showed minimal cardiomegaly and a grade II rough precordial systolic murmur with a questionable rub over the base of the heart was heard. Two fingersbreadth hepatomegaly was noted. The spleen was not palpable and there were no abnormal abdominal findings. Pelvic examination was within normal limits. There was sacral edema and 3 plus pitting edema of the feet ankles and pretibial areas. Reflexes were slightly hyperactive bilaterally. The patient responded only to painful stimuli. The plantar response was normal. There was no significant lymphadenopathy.

**Lab rotory St d es** Hematocrit was 42 per cent hemoglobin was 13 grams per 100 ml and the red blood cell count was 4 350 000 per  $\mu$ l. The white blood cell count was 8 000 per  $\mu$ l with 88 per cent neutrophils 11 per cent lymphocytes and 1 per cent basophils. The sedimentation rate was 42 mm per hr. Urinary specific gravity was 1.010 with 4 plus albumin no reducing substance and numerous red and white blood cells on microscopic examination. Blood urea nitrogen was 114 rising to 150 mg per 100 ml. Serum sodium was 107 rising to

125 mEq per liter serum potassium varied between 3.6 and 5.4 mEq per liter, chlorides rose from 12 to 76 mEq per liter.  $\text{CO}_2$  stayed between 17.3 and 18, mEq per liter. Calcium varied between 2.9 and 3.6 mEq per liter. Urinary output was noted to be between 425 and 525 ml per 24 hours. During electrolyte replacement the patient gained at least 1 3/4 pounds. The electrocardiogram was interpreted as "compatible with severe electrolyte disturbances."

**Course in Hospital** The patient remained comatose or semi-comatose until her death. She was given 200 ml of 5 per cent saline solution intravenously on admission but without clinical change. Penicillin and streptomycin were started. Another 300 ml of 5 per cent saline solution to which was added calcium gluconate was given on the second day again without improvement. On 5 May 1953 the morning of her death (3rd hospital day) the patient had a short episode of tonic and clonic movements of her extremities. Her blood pressure was stable at levels about 165/45 mm Hg with rare transient falls to values as low as 120 systolic. In the afternoon she again began to have convulsions, and 150 mg of Amytal Sodium (brand of amobarbital) was given by slow intravenous injection however the convulsion continued, and after 7 to 9 minutes the patient died.

## DISCUSSION

**Doctor Hoyle:** The illness of this 16-year-old white female dependent dates back to October 1952. Our records are not clear regarding that illness and up to the time of her admission in March 1953 but we know that she had nausea, vomiting, and generalized edema. She had an episode of vaginal bleeding in November 1952 and apparently a refractory anemia. She had signs and symptoms suggestive of renal failure and cerebral edema. She had had several tonic-clonic convulsive episodes. Examination on her last hospital admission showed unconsciousness, generalized edema, dilated pupils with "negative" fundi, questionable cardiomegaly, and a precordial systolic murmur of medium intensity. The liver was felt two fingersbreadth below the costal margin. At times she had a hypertension. Laboratory studies revealed a leukocyte count of 8,000 with 88 per cent neutrophils. Corrected sedimentation rate was 42 mm per hour. Urinalysis showed 4 plus albuminuria with frequent red and white blood cells. Blood urea nitrogen was 114 mg per 100 ml, sodium 107 mEq per liter, potassium 5.4 mEq per liter,  $\text{CO}_2$  18 mEq per liter, chlorides 42 mEq per liter, calcium 3.2 mEq per liter, urinary sodium and chlorides negative. X-ray showed increased bronchovascular markings. An electrocardiogram showed changes compatible with severe electrolyte disturbance.

In a 16 year old girl with nausea and vomiting *without* edema and with two and on half months of amenorrhea the possibility of pregnancy should be considered. However since she had the diffuse bleeding episodes one would think that she had miscarried if she had been pregnant.

Diagnoses of preeclampsia and eclampsia though rather rare before 24 weeks can be fairly well ruled out with the history of several profuse hemorrhagic episodes even with the provision that pregnancy pre-existed.

Also one must think of acute renal disease particularly acute glomerulonephritis in a individual of this age. The mode of acute onset of nausea vomiting and generalized edema would certainly suggest acute glomerulonephritis but we do not know what the urine findings were from October to March. We could speculate that she went through an acute episode of glomerulonephritis and continued to a terminal stage. This is a good possibility with the later physical and laboratory findings of renal failure with proteinuria hematuria azotemia and electrolyte imbalance. We do not know what the serum phosphorus was but the serum calcium was severely depressed. Acute glomerulonephritis remains a distinct possibility.

Another thing which should be considered regarding renal disease is a type of nephrosis or nephrotic syndrome. Nephrotic syndrome does not include cells in the urine to the extent we have in this case but there is some difference of opinion regarding this entity. She may have had a mixture of nephritic nephrotic disease. There is no evidence that she had previous chronic renal disease or previous hypertension.

Her course is one of a chronic nature in that it ran for five months before her admission in March 1953. During this time she was progressing neither favorably nor was she suffering any severe acute embarrassment. She had menorrhagia but it was not a course that one might see in clampsia if she were pregnant.

Let's think again along the line of chronic renal disease. I favor a collagen disease of the kidney either disseminated lupus erythematosus or periarteritis nodosa as the most likely diagnosis. Of these two possibilities I have attempted to compare and contrast the characteristics. The age at onset of lupus erythematosus is perhaps 15 to 40 versus 20 to 40 in periarteritis nodosa. Arthralgia and cutaneous lesions both are slightly more common in disseminated lupus erythematosus than in periarteritis nodosa. The patient demonstrates neither of these. Cardiovascular involvement is equally frequent. She has cardiovascular involvement. Hypertension is much more prevalent in periarteritis nodosa than in lupus. She has hypertension. Pulmonary lesions are equally divided. She has no pulmonary lesions except for increased bronchovascular markings. She has no pleurisy or effusion. Abdominal pain is more common in periarteritis nodosa. She does not complain of abdominal pain. Impairment of renal function

is more commonly found in periarteritis nodosa which she certainly shows. Peripheral neuritis and splenic enlargement are not present. Focal cerebral lesions are more common in periarteritis nodosa. Muscular inflammations are equally divided and she does not complain of this. As far as abnormal laboratory findings are concerned anemia is slightly more common in lupus although it is certainly found in both. The leukocyte count usually is elevated in periarteritis nodosa and usually depressed in lupus erythematosus. Her leukocyte count is neither depressed nor elevated. Eosinophilia is more common in periarteritis nodosa. No mention is made of an eosinophil count in the protocol. Abnormal urinary sediments are more common in lupus. LE preparation apparently was not done.

From these comparisons I favor periarteritis nodosa. I do not believe she shows any features of other types of disease with the exception of acute glomerulonephritis progressing to the terminal stage. I would diagnose this case as a type of renal insufficiency due to a collagen disease particularly periarteritis nodosa with the outside possibility of disseminated lupus erythematosus. Also one must consider acute glomerulonephritis which goes into a terminal stage.

Doctor Jernigan: You conclude therefore that she died from renal insufficiency primarily with periarteritis nodosa the first diagnosis followed in order of probability by disseminated lupus erythematosus and acute glomerulonephritis?

Doctor Hoffman: Yes.

Doctor Jernigan: Dr. Abrams, I would like to ask you to comment on the electrolyte imbalance. The electrolyte findings are unusual even for severe renal insufficiency. After she was admitted to the service hospital the blood urea nitrogen was 152 mg per 100 ml, the potassium was 3.6 mEq per liter, sodium 112 mEq per liter and the chlorides were reported as 69 mEq per liter. Also for the degree of insufficiency the  $\text{CO}_2$  was only 17.7 mEq per liter. How do you explain the low potassium if we assume that this is an accurate report?

Doctor Abrams: The presence of the low potassium is difficult to explain. There are two possibilities: (1) The patient is storing some potassium and (2) she is losing potassium just as he is losing salt. Of course the mechanism in the loss of salt is quite different from that in the loss of potassium and one of the things that causes an excessive loss of potassium is an elaboration of a larger than normal amount of aldosterone. The entire electrolyte imbalance is very confusing to me. I have been unable to explain it logically. The 3.2 mEq per liter of calcium initially and later reported as 2.9 and 3.6 mEq per liter is very striking. Of course low calcium is found in extensive

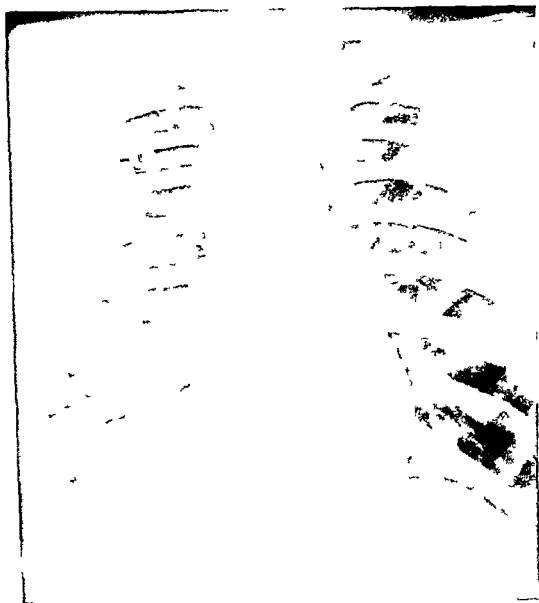


Cardiac fluoroscopy showed the mediastinal mass in question to pulsate. These pulsations were thought by the fluoroscopist to be transmitted rather than expansile in type. The examination was otherwise essentially noncontributory.



Figure 1. Retrograde catheterization of the superior vena cava (fig. 1) July 1956. The catheter was inserted through both the left and right internal jugular veins. The catheter was inserted into the superior vena cava.

An angiocardio-gram through the left antecubital vein (fig. 3) revealed the mass to be dilated superior vena cava. The left and right innominate, left subclavian and left iliac veins were similarly widened. There was suggestion of some narrowing of the upper or



*Figure 2 Roentgenogram on 26 July 1957 showing widening of the superior mediastinal shadow on the right*

vena cava central to the dilatation. No other vascular or cardiac abnormalities were demonstrated.

Venous pressure arm-to-tongue and arm-to-lung circulation times were normal.

Cardiac catheterization via the left antecubital vein disclosed normal pressures and oxygen saturation in the superior vena cava, inferior vena cava, pulmonary artery, right atrium and right ventricle. There was no evidence of caval obstruction or of cardiovascular anomaly.



Fig. 3. A graphic method of the peripheral axillary

Subsequently, mass survey photoroentgenograms of the chest taken in 1951 and 1952 were obtained (fig. 4). These showed a change in overall appearance of the right upper mediastinum when compared with the current studies.

The final diagnosis was idiopathic dilatation of the superior vena cava and findings probably congenital.

#### DISCUSSION

The normal superior vena cava is variable in size, ranging from 4.2 to 1.0 cm in length and from 8.0 to 20.0 mm in diameter. The mean diameter and length for 150 patients with no evidence

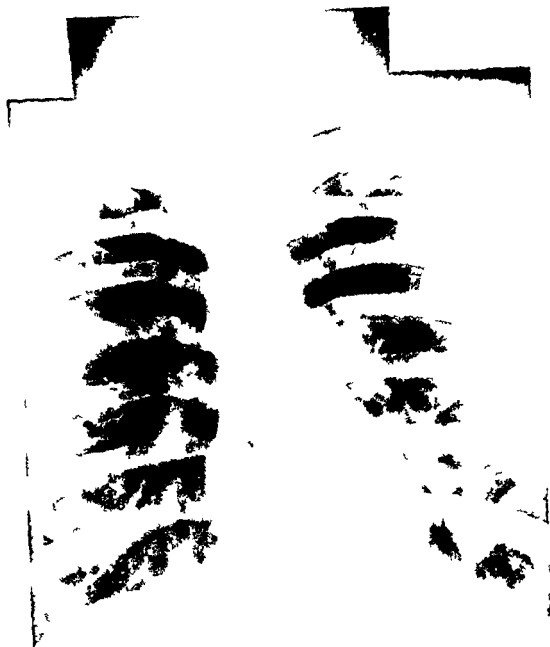


Figure 4 Photoroentgenogram on 19 February 1952 showing widening of the superior mediastinal shadow on the right present at that time

of abnormality was 14.8 mm and 7.7 cm respectively. The innominate veins show a similar variation.<sup>1</sup>

Dilatation of the superior vena cava and its tributaries has been related to saccular aneurysm of the superior vena cava, obstruction of the superior vena cava near the right atrium, right-sided heart failure, pericardial effusion, constrictive pericarditis, tricuspid insufficiency, and congenital cardiovascular anomalies producing increased pressure or flow within the vessel.<sup>1-4</sup> These

lesions upon thorough study will present characteristic findings which were not present in our case

On plain film and angiocardigraphic studies Abbott's case of aneurysm of the superior vena cava somewhat resembles the case reported here. Careful comparison of the two cases however reveals a number of dissimilarities

The complete absence of any significant findings associated with or related to the venous dilatation led us to the diagnosis of idiopathic phloectasia. Because of the diffuse nature of the abnormality and the lack of change over a long period of observation thoracotomy was thought unwarranted

This lesion is undoubtedly a most uncommon cause of mediastinal mass. It is thought, however that the case reported is of interest as an unusual abnormality. Furthermore it re-emphasizes the necessity for employment of every available diagnostic facility in the study of mediastinal problems prior to thoracotomy

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# Sulfapyridine in Dermatitis Herpetiformis

## Report of a Case Under 11 Years of Continuous Treatment

MERRIL M. COOPER *Leutenant MC USNR*

**S**ULFAPYRIDINE was first used in this country in 1928 in the treatment of pneumococcal pneumonia, for which it already had been found effective in England. In April of 1929 Costello<sup>1</sup> reported success with sulfapyridine in the treatment of a case of dermatitis herpetiformis (Duhring's disease) that had not responded to sulfanilamide or other medications over a four year period. His patient presented marked improvement in one week with complete clearing after two weeks of therapy, but a maintenance dose was required. After eight months of administering one half tablet every other day the patient remained clear.

Barling<sup>2</sup> later reported that one of his patients who had been started on sulfapyridine in 1929 for acute tonsillitis also had noted a great improvement in his dermatitis herpetiformis and had been maintained successfully on the drug for a four year period. During this span he was able on occasion to discontinue with sulfapyridine and remained clear of his dermatitis for a 4 week period after which time his skin would again erupt. Eventually he was maintained on one grain every 48 to 96 hours and would be relieved within 2 to 3 hours after reinstitution of therapy.

Senear and Perlstein were able to demonstrate repeatedly the efficacy of sulfapyridine in a five-year-old patient through deliberate cessations and reinstitutions of therapy with equally good results each time the drug was resumed. Brunsting<sup>3</sup> reported clearing in a 10 year-old patient after one week of therapy. His patient had been treated unsuccessfully for a 20 year period with other medications. As in other cases a maintenance dose was necessary.

In 1934 Swartz and Lever<sup>4</sup> compared the effect of sulfapyridine to that of sulfanilamide which previously had been found effective by Lain and Lamb. The comparative study of 13 patients revealed both drugs to be effective with sulfapyridine more effective and in smaller doses. All of the 13 patients

<sup>1</sup> M. P. Graduate Medical School of New York University, Bellevue Medical Center, New York City.

were benefited pruritus being considerably relieved within 12 hours and good improvement being noted 2 to 3 days after therapy was begun. Additional studies revealed that sulfathiazole had some beneficial effect whereas sulfadiazine and sulfaguanidine had none. More recently Everall reported on 17 patients 15 of whom he had maintained on an average dose of one and one half grams daily. Only one of these had failed to respond well.

Although it has been a general consensus that sulfapyridine is a good therapeutic agent in the treatment of dermatitis herpetiformis there are patients who cannot tolerate the drug because of side effects. These vary from slight nausea to agranulocytosis. Most commonly the patient will complain of nausea, malaise, vertigo or mental depression. Drug eruptions may develop. Molesworth was able to lower the dosage of sulfapyridine and maintain good results in 6 patients who could not otherwise tolerate the drug by giving folic acid 10 to 20 milligrams daily. He suggested that folic acid deficiency could be an important factor in causing toxic symptoms.

In patients who cannot tolerate sulfapyridine or who do not respond well to this drug the sulfones often prove beneficial. Promacetin (brand of acetosulfone), Diasone Sodium (brand of sulfoxone sodium) and the parent compound diaminodiphenyl sulfone have been used successfully. With use of the sulfones or of sulfapyridine regular and frequent blood studies and urinalyses are indicated.

#### CASE REPORT

A 56-year old woman with a five month history of an itching crusting eruption that began on the arm and legs and after 2 to 3 weeks became generalized was first seen in the private practice of Doctor Rudolf L. Baer in 1946. During the preceding five months she had received autoblood injections, roentgen ray treatments, various hormones and aromatic and other internal medications without improvement. On examination there were found up to palm-sized patches of grouped, excoerated papulovesicular lesions widely distributed over the entire body except for the face, neck, hands, feet and genitalia. Some hyperpigmentation was present in the subsiding and healed areas. There were coin-shaped eczematous plaques on the medial surface of the ankle.

In April 1946 the patient was given sulfapyridine three grams daily with sodium bicarbonate by mouth and a lotion containing menthol, phenol, crude coal tar and sulfur for topical treatment. Within one week her pruritus was about 80 per cent improved. She had much less pruritus and had developed no new lesions. The sulfapyridine was reduced to two grams daily but three days later because of pruritus was increased to three grams daily. This brought relief after three days at which time the patient noticed some fatigue.

Sulfapyridine was maintained at three grams daily until July, when it had to be discontinued because of a neutropenia. Seven days later, because of increased pruritus the patient was again placed on two grams daily with only slight improvement until she was given three grams daily. During the following 18 months she was maintained on two to three grams daily as needed for relief. On one occasion during this interval when the dosage was temporarily lowered to one and one half grams the eruption became more pronounced and spread to previously involved areas.

In February 1949 the patient was given a total of three injections at weekly intervals of Flo Cillin (brand of crystalline procaine penicillin G) receiving 297 grams (300 000 units) of penicillin at each injection. The penicillin was discontinued because of an intensely pruritic morbilliform eruption without any effect being noted on the original eruption.

During the following 20 months the patient was maintained adequately on one to two grams of sulfapyridine daily. The only episode of increased pruritus during this interval occurred after gradually reducing the dosage and discontinuing it entirely for one week. Several days after reverting to three grams of sulfapyridine daily the symptoms were relieved.

In October 1951 internal medication was discontinued again but was resumed after seven days because of increased pruritus. From January 1953 until July 1955 adequate control was obtained on one half gram daily but later in 1955 the dose was increased to one gram daily because of some crusting of the scalp that failed to clear on the lower dose.

The patient has been observed at intervals since then and was last seen in June 1957 while on one half gram daily. She is doing well but states that if she neglects taking a single tablet pruritus develops within 24 hours. The only other internal medication which the patient takes is one tablet of pyribenzamine daily. Regular blood studies have shown no toxic effects since 1946 during the third month of medication when the sulfonamide had to be temporarily discontinued.

## COMMENTS

During the entire period of observation, this patient has had an eosinophilia. This was 6 per cent of the total white blood cell count at the time she was first seen, whereas subsequent blood examinations have shown as high as 27 per cent. There has been no apparent relationship of the degree of eosinophilia to the dosage of sulfapyridine. The neutropenia that became evident during the third month of medication while on 2 grams of sulfapyridine daily has not been manifest since, although comparable doses have been given for short periods.



The response of dermatitis herpetiformis to sulfapyridine is difficult to interpret as neither the mechanism of action in this disease nor the etiology of the disease are known. It is unlikely that an antibacterial action against the disease itself or against a focus of infection could offer a satisfactory explanation considering that dosage as small as one half gram daily may be sufficient to control symptoms and clinical manifestations over prolonged periods.

### SUMMARY

A patient with dermatitis herpetiformis has been maintained on sulfapyridine for 11 years with complete control of all symptoms and clinical manifestations. Side effects have been minimal and there are no demonstrable ill effects from the prolonged medication.

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# Alkaptonuria

DAVID MARSHALL *Captain USAF (MC)*

**A**LKAPTONURIA is a disorder of protein metabolism characterized by the excretion in the urine of large amounts of homogentisic acid, an intermediary substance of tyrosine metabolism. Presumably the body lacks a specific enzyme or enzyme system for the catabolism of homogentisic acid. This defect is thought to be hereditary, inasmuch as there is a definite familial tendency to this disease.

The entity of alkaptonuria attracts the attention of the clinician because of its rare occurrence and the dearth of existing information about this disease. Only slightly over 200 cases have been reported in the literature, and the disease is rarely encountered, even in a general hospital.<sup>1</sup> Consequently, it is believed that the occurrence of another case should be noted in the literature, and the fact that this case was seen at a U S Air Force Dispensary points up the importance of keeping this entity in mind wherever medicine is practiced.

## CASE REPORT

A 32 year old aeromedical specialist at this facility reported for an annual physical examination and in the course of this submitted a urine specimen. The laboratory was busy and the specimen was left overnight only to be found colored black in the morning. The possibility of alkaptonuria was entertained and analysis of the pint specimen revealed 20 mg percentage of homogentisic acid.

The past history and review of the systems was unremarkable and the patient was in good health. There had been no complaints of arthritis or other symptoms. The general physical examination revealed no abnormalities. There was no evidence of pigmentation of the scleras, cartilages of the ear or other parts of the body.

A complete blood count, urinalysis, chest and lumbosacral spine films and serology test were all within normal limits and all previous urinalyses were reviewed and found to be negative.

The patient's family, consisting of one brother, two sisters and parents, were queried in correspondence and none of their urine specimens was observed to turn black or brown after standing for 24 hours.

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## DISCUSSION

## Tests for Detection of Homogentisic Acid in Urine

Most of the tests described are nonspecific and several are reported as giving a false negative result. The most reliable test of course is the determination by isolation. Chromatography, which is a simpler procedure than isolation, is probably more feasible and next most reliable. The remainder of the tests described give varying results and all were negative in this case except for the oxidation test.

*Oxidation test* The urine turns dark on standing. This occurs supposedly because homogentisic acid polymerizes during the process of oxidation, becoming a black or brown black pigment. It should be pointed out that porphyrin, melanin, and possibly phenolic compounds can give a dark urine on standing and should be ruled out.

*Sodium hydroxide test* An alkaline urine hastens the process of oxidation and therefore this is an elaboration of the oxidation test.

*Benedict's test* Homogentisic acid causes a reduction of copper salts in alkaline solution.

*Ferric chloride test* The addition of a few drops of ferric chloride produces a transient blue color.

A drop of alkaline urine placed on a sensitized photographic paper causes the immediate appearance of a black spot on the paper.

Other tests which are nonspecific have been described in the literature.

This relatively asymptomatic disease usually is noted in childhood when diapers or undergarments frequently stain black. It is stated that approximately 50 per cent of all patients with alkaptonuria go on to develop ochronosis—an entity characterized by the deposition of pigment in the cartilaginous areas, most commonly the joints, and giving rise to the symptoms of arthritis. This occurs most frequently in the third or fourth decade and most commonly involves the joints of the spine. The exact nature of the pigment is unknown though it is believed to be formed from homogentisic acid. Except for this complication, alkaptonuria is a benign disease with no effect on longevity.

An important and confusing effect of the disease is its ability to cause a false positive test for glucose in the urine by reducing Benedict's solution. Consequently the development of an atypical or black precipitate when doing a Benedict's test should make

one third of this disease. In addition, a patient in the third or fourth decade who complains of arthritic symptoms also should alert the clinician to rule out ochronosis by testing the urine for the presence or absence of homogentisic acid.

There is no known treatment for alcaptonuria. The disorder has been produced in some normal humans and in experimental guinea pigs by feeding them a diet deficient in vitamin C, accompanied by oral doses of tyrosine. When vitamin C then was supplied the homogentisic acid disappeared from the urine. However, to the author's knowledge, no clinical case of alcaptonuria has been affected by the administration of vitamin C.<sup>5</sup> Cortisone has been used orally in an effort to alter the basic metabolic defect with no change in the urinary output of homogentisic acid in an alcaptonuric; however, one patient with ochronosis did develop a decrease in the urinary output of pigment on cortisone, accompanied by relief of arthritic symptoms, with recurrence of symptoms when cortisone was discontinued.

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## DR BERRY HONORS TURKISH HERO IN ANKARA GIVEN MEDAL OF HONOR IN PARIS CEREMONY

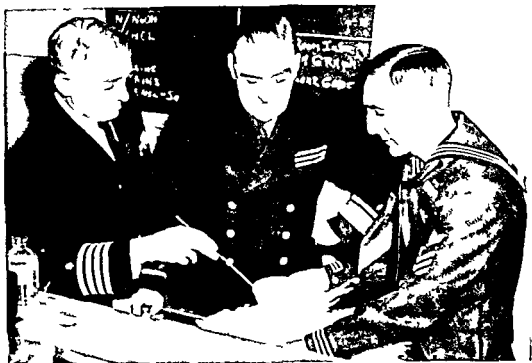


Dr. Frank B. Berry, Assistant Secretary of Defense (Health and Medical) and Major General Tevfik Gu r Surgeon General of the Turkish Armed Forces (above) led a delegation of civilian and military physicians to Ankara to place a wreath on the tomb of Ataturk for the president of the Turkish Republic during the second Armed Forces International Conference on Nutrition 14-15 and 16 April 1958.

Below Dr. Berry (second from left) is shown wearing the French Army's *Médaille d'Homme du Service de Santé en Or* awarded to him at the banquet in his honor at Val de Grace Hospital in Paris by Major General Alfred R. Linger (left), Inspector General of the French Military Medical Service. To the right of Dr. Berry are Major General Raymond Debenett, Surgeon General of French Armed Forces; Major General William H. Powell, Jr., USAF (MC) Chief Medical Officer of SHAPE; and Dr. J. P. Byrne, president of the Association of Military Surgeons of France. Usually awarded posthumously, Dr. Berry received the medal for his aid to the Free French Army in World War II. It has been given to living persons on only three previous occasions.



## ADMIRAL HOGAN TOURS NAPLES, MEETS PETE



During a recent tour of U S Navy medical facilities in Naples Rear Admiral Bartholomew W Hogan Surgeon General of the Navy met Pete a white leghorn rooster whose blood is used in testing Mediterranean area influenza strains at the Navy s Preventive Medicine Unit No 7 Shown above from left to right are Captain Van C Tipton MC USN officer in charge of the unit Admiral Hogan Hospital Corpsman first class W J Steeger and Pete

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### Annual Anesthesiology Meeting 7 12 July

The fifth annual Anesthesiology Review Session of the Armed Forces will be held at the U S Air Force Hospital Lackland Air Force Base Tex 7 12 July 1958 The instructors panel for the meeting includes John Abajian Jr M D University of Vermont College of Medicine Charles R Allen M D University of Texas School of Medicine Raymond F Courtin M D Baylor University Hospital Dallas Tex George W N Eggers M D University of Texas School of Medicine and Major Joseph T Melton USAF (MC) Lackland Air Force Hospital under the presidency of Brigadier General Robert E Lee USAF (MC) Surgeon Tactical Air Command The society was organized in May 1957 to foster the advancement of the art and science of surgery in the Air Force and to encourage clinical and laboratory investigation of various problems of surgical significance

## A MESSAGE FROM THE A M A

The article this month will consider the problems of that rapidly growing population group in the United States our senior citizens. The aged population of the United States has increased by over 11 500 000 persons since the turn of the century. In 1900 there were 3 080 000 persons 65 years of age and over. It is estimated that there now are 15 000 000 persons in this age group. While the population as a whole doubled during this period, the number 65 years and over has quadrupled. By 1975 it is estimated that there will be 21 000 000 to 23 000 000 persons in this group, but as a per cent of total population it is leveling off at about 9 to 10 per cent.

However, as the size of the older age groups increases in overall numbers, the problems which confront older persons assume more importance for those directly and indirectly affected. New problems that occur in the health, emotional, social, economic, and psychologic areas of the lives of all persons are intensified in the older person. While other age groups in the population have the flexibility to rebound from some of these problems, the aged must adjust to a series of limitations that have arisen in the past decade or two. The aged person must learn to accept his physical and mental disabilities or limitations, to face possible retirement due to inflexible retirement policies, although he is able to carry on his work adequately, to face the loss of prestige and satisfaction of a job accomplished well, a decrease in social participation, the continuing loss of his relatives and contemporaries, and change in his mode of living brought about by persons and possibly himself thinking he is old and therefore of little use.

Even though this is a growing mass problem of some 15 000 000 individuals, the significant factor lies in how a person adjusts to this change of his style of living. His ability to adjust is based on his emotional and psychologic background. Students of mental change in the aged believe that the basic patterns of response in older persons remain essentially the same as their reactions to the stresses and frustrations of life in their working days.

These individual adjustments to change must be accomplished as quickly and as smoothly as possible. Although these individual problems must be answered when we consider the problems of the aged en masse, we are confronted with vaguely discerned out-

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—Editor

lines of their social, psychologic, and economic status due to the increase of numbers in the last two decades. It would appear that everyone with an aged parent or relative is an "expert" on the aged. But the aged is not a static group, it is one of the fastest growing population groups, and while numerous research projects have been carried out on the problems of the older person, these surveys were normally made of a population that existed in the Great Depression of the 1930's or closely following the controlled economy of the war period. These surveys produced answers that are almost too pat, namely, old people are lonely, they must adjust to widowhood, they must live on reduced income, they suffer from a feeling of uselessness, they no longer have a role in society as a worker or a homemaker, and they are subject to increasing infirmity and disability.

We tend to accept without analysis. When the aged were a less significant number in our population, attention was placed by the medical profession on meeting the prime problems of medical care, that is, taking care of the growing family with provision of care for the child, the maternity case, and the acute episode. Such a policy was followed in the construction of most general hospitals. Such a policy was followed by the voluntary health insurance industry. Concentration was on taking care of the *main* medical problems. Now, that huge strides have been taken, the medical profession has been able to concentrate more research time and energy on the multiplying problems of the aged and other growing population groups.

Always interested in the problems of the aged, the American Medical Association had established a Committee on Aging as one of the committees of its Council on Medical Service. In the last two years much of the existing information on the socio-medical problems of the aged has been gathered. A series of regional meetings has been held to acquaint the physicians with the newest trends among the aged. In part on the basis of this work, to prevent any additional growth in problems of the aged, four medical organizations—the American Dental Association, the American Hospital Association, the American Nursing Homes Association, and the American Medical Association—have banded together to improve the health care of the aged. These organizations initially wish to find the answer to two main questions. In an era of improved surgery, tranquilizers, and finer hospitals and facilities what are the sociomedical problems of the aged? And, what has happened since health surveys were made in the 1930's? Once we have a clearer understanding of the medical needs and the demands of the aged, we can urge proper policy to meet such needs. Simply to rely on small out-of-date samples will not lead to meaningful aid to the aged.



# OFFICERS CERTIFIED BY SPECIALTY BOARDS

## Supplementary Listing

The Surgeons General of the military medical services have announced that the following regular Medical and Dental Corps officers have been certified by the boards indicated since the listings published in previous issues of the *Journal*

### American Board of Pediatrics

H ward H J h J C pt USAF J ph G R i Lt USN

### American Board of Psychiatry and Neurology Psychiatry

Ch l E H lily Lt C mdr USN

### Neurology

Th d M B dgl y M J USA

### American Board of Orthopaedic Surgery

J m T L l J M J USAF J h F Tra y M J USAF  
R g A Sta dard C pt USN

### American Board of Dermatology

H nry T A b C md USN W l l m G L w C pt USN  
E P K h C p USN

### American Board of Urology

Alb A G l k C pt USN J k R R b M J USAF

### American Board of Internal Medicine

Orv ll F N l C mdr USN G g H Tarr C pt USN

### Gastro nterology

J m T Hardy L C l USAF Emm tt L K h C l USA

### American Board of Pathology

J Th t B w ll L C mdr USN F J M M h C p USN  
J h F M Cab C p USN

### American Board of Ophthalmology

J h E. G ll L C md USN

### American Board of Otolaryngology

F c J Sw y L USN

### American Board of Surgery

H m S. Ar ld L C md USN L ry J H Lt C mdr USN  
N ll H B k M USAF R b tt B J m J C pt USN  
Mark T C M USA W t C. J m L C l USA

### American Board of Surgery—Continued

Arthur Cohen Lt C I USA

Donald G F by Lt Col USA

Robert J Fleischaker Comdr USN

Philip O Geib Comdr USN

Robert C L ning Lt Comdr USN

Edmund Scavo e Lt Col USA

Hor ce D Warde Capt USN

### Board of Thoracic Surgery

Philip L Nov C pt USN

### American Board of Anesthesiology

B sel M Mix Jr Maj USA

### American Board of Neurological Surgery

J seph A Witt Lt Comdr USN

### American Board of Periodontology

Wilfr d B Bell M J USA

H rb rt B L fette Lt C I USA

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## Central Repository for Medical Credentials

The Secretary General of The World Medical Association has announced that on 1 July 1958 the services of a *Central Repository* for Medical Credentials will become available to the doctors of the world. All judicious precautions will be exercised to protect the records of depositors.

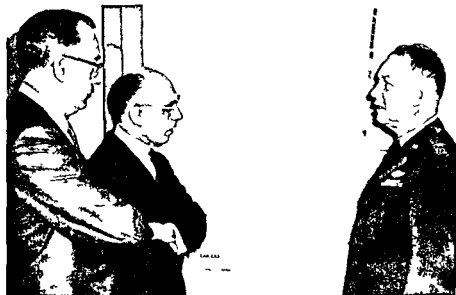
During war and national uprisings medical records are destroyed or lost. The plight of hundreds of doctors who fled from their homelands during World War II and the more recent Hungarian uprising stimulated The World Medical Association to undertake means assuring the doctor that he will always be able to prove himself medically trained and fully accredited to practice medicine. Today many doctors are working as laborers or research assistants as a result of the loss or destruction of their original credentials and the lack of a protective service in which authenticated copies could be deposited.

The lifetime cost of the service on a one payment basis to the newly graduated doctor is approximately \$60.00 (USA). An actuarial schedule has been established for doctors in the various age groups. A 10-year service rate is also available.

The officials of the Repository recommend that doctors deposit their credentials in a form legally acceptable in the country or countries in which they would desire to establish themselves as qualified to practice medicine. It suggests that the credentials so deposited include official medical school record, medical diploma and specialist credentials.

Additional information on the Central Repository for Medical Credentials is available from The World Medical Association, 10 Columbus Circle, New York 19, N. Y.

# AIR FORCE CONSULTANTS VISIT USAFE



Doctors Frank E. Stinchfield and Carlos G. de Gutierrez Mahony of New York City national consultants to the Surgeon General of the Air Force receive a briefing from Brigadier General Harold H. Twitchell, Surgeon of U. S. Air Forces in Europe. The consultants were accompanied last month on the tour of Air Force medical facilities in Europe by Colonel Frances L. Ly of Washington Air Force Chief Nurse.

## DEATHS

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## Reviews of Recent Books

A TEXTBOOK OF CLINICAL NEUROLOGY With an Introduction to the History of Neurology by *Israel S. Wechsler* M D 8th edition 787 pages 179 illustrations some in color W B Saunders Co Philadelphia Pa 1958 Price \$11

This is the eighth edition of a book on clinical neurology which has enjoyed a rather widespread popularity on the American neurologic scene for the past 30 years. Nevertheless in the opinion of this reviewer the eighth edition is somewhat disappointing from the standpoint of being considered a major revision.

Although there are many excellent sections in this work particularly the sections on neurosyphilis epilepsy and aphasia there are other sections which would seem to this reviewer somewhat sketchy for such a specialized textbook. While it is realized that the arrangement of a textbook is discretionary with an author there are some aspects of this work which in the opinion of this reviewer would tend to confuse the student. An example of this is the listing of amyotrophic lateral sclerosis with the spinal cord diseases and the lack of emphasis of the relation of this disease to progressive muscular atrophy which is discussed in a section on neuromuscular disorders and myopathy. While many of the sections have been revised many others are incomplete with regard to bibliographic references which in some cases show no contributions later than 1948. In the case of amyotrophic lateral sclerosis and progressive muscular atrophy for example the work of Doctors Mulder and Kurland on the hereditary nature of these disorders has not been mentioned.

The hereditary disorders are rather sketchily treated and it is thought that their variants are discussed in insufficient detail considering the specialized nature of the material dealt with. Olivopontocerebellar atrophy is placed in a different section than hereditary disorders and the definite statement is made that this is not an hereditary condition notwithstanding the fact that a family pedigree in which postmortem material associated with clinical manifestations were discussed in which this disorder appeared as a clear cut hereditary familial manifestation in a recent article.

While the section on syphilis of the nervous system is generally rather good the discussion on tabes is described as an entity usually presenting little difficulty in diagnosis. This certainly is not in accord with the experience of most clinical neurologists these days. This disease is extremely subtle in its manifestations and because of its increasing rarity often presents an unusual degree of diagnostic difficulty particularly in the absence of positive serologic reaction. In regard to diagnostic tests for syphilis no mention is made of the importance of the use of the treponema immobilization procedure which has been shown to be of considerable aid in the diagnosis of doubtful cases. Fever therapy which is recommended in this edition

as being a desirable treatment of cases of general paresis is controversial at best

In addition to the above criticism it is noted by this reviewer that there is a rather long section in the book devoted to a discussion of the neuroses a feature which would seem to this reviewer rather anachronistic in a modern neurology textbook This chapter is rather well written and though rather long can still hardly cover the ground adequately for the student of neurology In the opinion of this reviewer this space could have been much more profitably devoted to the expansion of some of the more purely neurologic sections of this book

In summary it is the belief of this reviewer that this volume will be accepted with considerable ambivalence by the specialty of neurology particularly in view of Dr Wechsler's significant contribution to the advancement of the study of neurology over the year as a clinician teacher and a theorist Unfortunately however an objective evaluation of this work would seem to indicate that it does not come up to many of the textbooks on neurology which have been published here or in Great Britain during the past several years

—ROY E CLAUSEN J L C I MC USA

5-HYDROXYTRYPTAMINE: Proceedings of the Symposium held in London 1st and 2nd April 1957 edited by G P Llewellyn Jones PhD 253 pages Illustrated Pergamon Press New York N Y 1958 Price \$9.50

This is a well published and illustrated symposium of a remarkable meeting held to discuss the findings of research concerning 5-hydroxytryptamine

In one sense this small volume shows the evolution of thinking in a particular field of pharmacology This field was introduced a number of years ago with the concept of sympathin E and sympathin I In this symposium the rapid evolution of such concepts is made apparent by use of the newly hypothesized trophotropic and ergotropic divisions of the autonomic nervous system Regardless how controversial such a system is it is a convenient scaffold on which may be built workable basis of research concerning the central and peripheral nervous systems

The discussion of 5-hydroxytryptamine is thorough regarding its central and peripheral actions however all the discussions concern research animals Nevertheless any clinician may rapidly integrate this research material into a workable understanding of the causes of the symptoms accompanying this syndrome labeled carcinoid

This small publication will be most useful to researchers in the fields involving 5-hydroxytryptamine All other physicians however should be aware of the scope of research involving exogenous and endogenous substances affecting the central nervous system This volume should be included in all large medical libraries

—EDWARD J HUYCKE Capt. MC USA

**PREVENTIVE MEDICINE FOR THE DOCTOR IN HIS COMMUNITY** An Epidemiologic Approach by *Hugh Rodman Leavell* M D Dr P H and *E Gurney Clark* M D Dr P H and 19 contributors 2d edition 689 pages McGraw-Hill Book Co Inc The Blakiston Division New York N Y 1958 Price \$10

In this second edition the contributors have retained their purpose of presenting a text directed toward the development of a point of view and the application of epidemiologic methodology to disease and accident prevention. Health promotion is emphasized. Chapters have been rearranged and grouped into three sections as follows: Basic Principles, Application of Principles, and Public Health Preventive Medicine as Organized Community Action. The increasing importance of dentistry in health promotion and community health programs has been recognized by the inclusion of a new chapter on the Natural History and Prevention of Oral Disease. Many new diagrams and illustrations have been added and the text has been brought up to date.

Diseases, disorders and conditions are discussed with the concept in mind that they are the result of multiple causes acting through the agent, the host, and the environment. The natural history of the condition is presented and application of preventive measures discussed. Such measures as health promotion and specific protection are applied at the prepathogenesis period; early diagnosis and prompt treatment, disability limitations, and rehabilitation are measures applied during the period of pathogenesis. The discussion of these concepts is made more lucid by well arranged diagrams.

One of the purposes of this book is to point out the value of practicing medicine with the preventive point of view and this is well done throughout. For the benefit of those who wish more detailed information, references are provided at the end of each chapter and a list for additional reading at the end of many.

This volume should be especially helpful to medical and dental students, practitioners and teachers of public health, and those general practitioners who wish to integrate preventive into the general practice of medicine. —*HOWARD A. SESSIONS* Capt MC USA

**PARENT CHILD TENSIONS** by *Be thold Eric Schwarz* M D and *Ba thol omew A Ruggieri* M D 238 pages J B Lippincott Co Philadelphia Pa 1958 Price \$4.95

In *Parent Child Tensions* Dr Schwarz and Dr Ruggieri have written an extremely interesting book on the problems of children. The first four chapters deal with the dynamics of normal emotional growth and development and are cleverly illustrated with quotes from suitable cases. In fact the whole volume is rich with nontechnical illustrative case material and reads like a popular book.

The next 12 chapters deal with specific psychiatric psychosomatic and behavioral conditions such as enuresis, tics, temper tantrums,

asthma various fear delinquency and sexual problems The remainder of the book is devoted to a variety of situations one encounters in pediatrics and practice in general such as the child's emotions before and after surgery emotional problems of hand capped children feeble-mindedness death and divorce in the family and special problems regarding adoptions

The authors are obviously well qualified and practical minded specialists in pediatrics and psychiatry and have done an excellent job of combining their observations experiences and treatment techniques into a readable and nontechnical volume It is intended in part as a helpful guide for rearing well adjusted children and has been recommended for physicians parents and parent-to-be The early chapters dealing with problems of the handicapped death divorce et cetera may well serve that purpose but I have strong personal reservations as to the usefulness of this book or any book that attempts to give parents an understanding as to the role their own disturbed feelings play in the genesis of emotional disturbances in their children We find that we are dealing usually with neurotic parents and intellectual explanations alone unfortunately are not very effective It is hoped however that this book may influence the parents who need help in this field to seek it

I enjoyed reading *Parent Child Tension* and compliment the author on an informative as well as an enjoyable book I recommend it to physicians social workers ministers teachers counselors and with some reservations to parent and parent-to-be

—STEPHEN MOURAT Lt C L MC USA

THE BACTERIOLOGY OF TUBERCULOSIS by Eg D r s M D 488  
 p g s 11 tr t d U ty f M an ta P s M an pol M an  
 1958 P \$10

This monograph presents an exhaustive survey of the literature of the bacteriology of tuberculosis from the late nineteenth century to the present day

The objective of the author is to present a thorough understanding of the etiologic agent of tuberculosis so that the investigator may fix a historical complete conquest of the disease Dr Darzins has done this through presentation of the material in historical sequence with an extensive bibliography consisting of abstracts from some 252 current periodicals

This book written primarily for the research specialist in tuberculous bacteriology and such is a shining example of scientific reporting Because of its limited area it will not appeal to the Medical Officer in the field but should serve as source reference for the research worker the investigator and the phthisiologist

—CHRISTOPHER C SHAW Capt MC USN

Symposium on DISEASES AND SURGERY OF THE LENS Transactions of The New Orleans Academy of Ophthalmology 1956 edited by George M Haik M D F A C S and Elizabeth M McFetridge M A Art Editor Don Alva do 260 pages illustrated The C V Mosby Co St Louis Mo 1957 Price \$10.50

Modern ophthalmologic symposiums are performing a great service by making available to the practicing ophthalmologist current teaching of the masters in the diagnosis and management of various problems and the Symposium on Diseases and Surgery of the Lens is an excellent example published in book form

The round table discussions of problems in each disease category are very enjoyable and provide the answers to many questions which only mature judgement and experience can answer The failure to include a section on the normal and pathologic physiology of the lens is regrettable but perhaps is circumstantial evidence that very little is known of this subject This book should be a must for every resident and ophthalmic surgeon —JOSEPH M JORDAN Capt MC USA

PRINCIPLES OF IMMUNOLOGY by John E Cushing and Dan H Campbell 344 pages illustrated McGraw-Hill Book Co Inc New York N Y 1957 Price \$6.50

Immunity to disease has been the major stimulating factor in the development of the science of immunology The techniques and concepts of immunology however are not restricted to medicine and they provide a tool for the study of other biological problems population genetics embryological development fertilization and antigenic individuality The authors of this book have focused their attention upon these latter problems and have produced an extremely readable interesting and stimulating treatise They have devoted eight pages for example to natural antibodies in humans other vertebrates in vertebrates and plants but only a sentence to the more mundane Wassermann antibody

The tremendous amount of information which the immune response has contributed to the attempted solution of biological problems has been assembled and interpreted in this book Because it covers vast areas of the subject experts in any particular field may not agree with some portions of the treatment made in the interest of simplification and condensation Jerne's recent natural selection theory of antibody formation is stated merely to represent a revival of Ehrlich's receptor theory That is partly true but Jerne's theory goes much beyond Ehrlich's concept and has certain advantages over other current theories of antibody formation This type of criticism could of course be leveled at almost any textbook

Finally this book is very valuable for students because it is characterized by an emphasis on principles rather than on the enumeration of data Its excellent references to the original literature also enhance its value —LOUIS H MUSCHEL, Maj MC USA



ACCEPTED DENTAL REMEDIES 1958 Drug d D tal P tic  
 l d g L t f B and cep d by th C un l De t l Th ra  
 p t c f th Am an D tal A oc t 23d dt on 214 p g  
 Am i an D t l A t on Ch c g III 1958 P \$2

Less than half of this useful book deals directly with medicaments. The rest is a valuable interesting account of allied factors in dental treatment other sections are a pertinent and interesting account of allied factors in dental treatment. The chapter on Dental Considerations of Patients Receiving Medical Care is phrased in the language of a round table discussion. It is a good exposition of current practices as opposed to outmoded textbook thinking. Another pertinent section concerns the Treatment of Emergencies.

A section on Nutrition includes daily requirement charts and a bibliography. The accepted drugs are covered by description action uses and source. Those not approved or with approval pending also are listed. This review reference volume is inexpensive practical and desirable.—JULES D. KARTMAN Lt Col USAF (DC)

Th Phy l g B f GASTROINTESTINAL THERAPY S l ct d T p  
 by H b N b l M D Ph D F A C P d M t M  
 A b M D F A C P 330 p g Grun & St tt I N w  
 Y k N Y 1957 P \$8.75

The authors of this slender volume believe that The teaching of gastrointestinal physiology seems to be too cursory and inadequate for the understanding of the disturbances of normal processes. They have therefore provided a review of the subject with emphasis on the physiological alteration in disease states and the changes that may be brought about by therapy. The first half of the book contains chapters on innervation motility drug effects secretion and digestion and absorption and secretion. The latter portion covers liver and gallbladder and pancreas.

The style is double the material well presented. All important subjects are covered and the correlation with clinical practice is excellent. This is not a textbook on physiology however and the discussions are presented as conclusions with very little background explanation or experiment. No diagrams chemical formulas or illustrations interrupt the steady flow of concentrated distilled description. There are many references included so that if one wishes more detailed information he will know where to find it.

At first glance this brief synopsis approach may seem disadvantageous. Few readers however would find the time to read a heavier more exhaustive and less conclusive text. This is a book for the medical student who needs to learn the relationship between the demonstrations in the laboratory and the symptoms of patients seen in the clinic. It is also a book for the practicing physician who needs to be reminded of the physiology basis of many gastrointestinal complaints and for all of us who need to be brought up to date on new developments and changing concepts.

—BENJAMIN H. SULLIVAN J. C. L. MC USA

MOSBY'S REVIEW OF PRACTICAL NURSING by Dorothy Kelley Rapier  
R N B S. et al 2d edition 354 pages illustrated The C V Mosby  
Co St Louis Mo 1957 Price \$4.25

This review will be of value for the practical nurse as preparation for licensing examinations if it is used as described by the authors who state that "the material should be used in conjunction with text books or reference books. References from current texts are listed for each unit as an introduction after which there is a comprehensive outline of the entire unit as it is approached by the practical nurse. Following each unit there are examination questions of various types: completion, matching, and multiple-choice questions with answer sheets included. Since the technique of taking an objective examination can actually be the downfall for one who otherwise knows the subject, these examinations should be of assistance in directing the student's mental exercise and should serve as a stimulus and challenge to further study.

The units are tailored to the curriculum suggestions of the National Association of Practical Nurse Education and will be a consistent transition for the student to carry her thinking from a current accredited program on to the usual types of state registration examinations for practical nurses.

It is thought that there can be a definite hazard in the use of such a book by any other than one who is already qualified by a breadth of good learning experiences. For instance, in the unit Basic Nursing Care, it might be possible for one to assume the necessary knowledge of a procedure by only the four to five steps given in the outline when there is not the background realization of necessary precautions and understandings. This danger is also inherent in the unit on medications of course.

There are a few unfortunate errors; for instance, the statement that the District of Columbia had licensing laws for practical nurses in 1955. There also are a few disturbing errors in outline format and the detail in the outline on body structure is not reasonable for a practical nurse. It is believed that this book is of value for the specific group for which it is intended if it is used with intelligent discretion.

—DELZENA E. GARRARD Maj. ANC USA

PHARMACOLOGY AND THERAPEUTICS: A Textbook for Students and Practitioners of Medicine and Its Allied Professions by Arthur Gollman, Ph.D., M.D., F.A.C.P. 3d edition 1046 pages 192 illustrations 2 in color 35 tables Lea & Febiger Philadelphia Pa 1958 Price \$12.50

In the past several years two of the classic textbooks of pharmacology in this country have been revised. Gollman's new edition worthily places it in this category. The printing is superb and it is pleasant to have a 1000 page book which is not too heavy to hold and handle comfortably. The type face and the use of boldface letters make the text easy for both study and rapid scanning. It obviously

is written for medical students taking pharmacology in their first or second year. Therapeutic uses of the drugs discussed is very sketchy but reasonably well cross indexed. The third edition is adequate in covering newer drugs such as tranquilizers and chemotherapeutic agents for malignancies but it is difficult to understand why so much space is given to such drugs as strychnine and nicotine while three short paragraphs are given to ethyl ether. Apparently when the first pharmacology texts appeared the use of such drugs as strychnine and nicotine were mentioned at length to help define the physiologic and pharmacologic boundaries of drugs. Such pharmacologic studies are well discussed in general physiology now.

This text is not detailed enough nor does it give enough reference material to be useful in graduate teaching of pharmacology. At the end of each chapter is a list of USP drugs with their doses. The addendum to each chapter will be highly useful to house staff officers and practitioners because it should remind them that almost all pharmacologic agents can be secured from the USP listing.

The bibliography at the end of each chapter appears adequate for medical students and practitioners. This book is recommended for general medical libraries and medical student.

—EDWARD J. HUYCKE Capt MC USA

THE YEAR BOOK OF DRUG THERAPY (1957-1958) (Book Series) edited by Henry B. Kman M.D. 518 pages. Illustrated. The Year Book Publishers, Inc. Chicago Ill. 1958. Price \$7.50.

This excellent collection of abstracts of the more important recent articles selected from American and foreign journals pertaining to drug therapy is well organized and well presented. Drug therapy in a wide variety of disease conditions is reviewed and current trends in therapy are described. The abstracts of the original articles contained in this book are brief, concise, accurate, clear and are read with ease. Current experience and trends in the treatment of various neoplastic diseases by drugs are discussed and recent concepts on the use of corticotropin and the corticosteroids are adequately reviewed. Various new antidiabetic drugs are discussed presenting the methods and results of clinical employment as well as the mechanisms of action. The book summarizes current drug therapy for all major disease entities particularly those which have been recent advances.

The references for the original articles abstracted in this book are conveniently printed as footnotes on the page on which the summary appears. Illustrations are black and white and include graphs, charts and photographs which assist the reader in understanding the material.

This book is a necessity for all internists and general practitioners and is an excellent summary of the recent literature relating to drug therapy and will serve as a source of ready reference for medical students. —RALPH D. ROSS Capt MC USN

URINE AND THE URINARY SEDIMENT A Practical Manual and Atlas by Richard W. Lippman, B S M D 2d edition 140 pages 92 color photographs Charles C Thomas Publisher Springfield Ill 1957 Price \$8.50

This is an excellent manual and atlas on urinary sediment of special interest to those working in clinical laboratories and in the field of internal medicine. Urologists also can gain considerable information from it regarding the findings in urinary sediment. The first of three chapters covers proteinuria and elements of the urinary sediment; the second, clinical applications of the observations of the urine in disease; and the final chapter gives information regarding qualitative and simplified quantitative methods. While the author encourages the use of quantitative methods, it is recognized that qualitative means are necessary for practical screening purposes. Written in brief terse descriptions, this is a unique guide to the identification of formed elements in the urine and their significance. It is well illustrated and contains excellent colored microphotographs.

—JOHN A. SCHINDLER Col USAF (MC)

GENERAL DIAGNOSIS AND THERAPY OF SKIN DISEASES An Introduction to Dermatology for Students and Physicians by Hermann W. S. Semens M D Translated from the German edition by Kurt Wiener M D 324 pages illustrated. The University of Chicago Press Chicago Ill 1958 Price \$10

This is the first English translation of a German text published originally in 1952. It is primarily a treatise on the fundamentals of dermatology. It is broadly divided into two sections: one on general diagnosis and the other on general principles of therapy.

The subject matter is handled in an informal narrative fashion and is not difficult reading. There is, however, a tremendous amount of information presented, much of it of practical importance. Most of the illustrations are close ups and of unusual clarity.

One could make minor criticisms, such as too much splitting of hairs on minor details and the introduction into an already overburdened dermatologic nomenclature additional synonyms for known entities. The author takes opportunity to proclaim four such synonyms and in addition labels them with his own name. This custom of adding eponyms to medical literature is not only unscientific but actually harassing to medical advance.

This is not a book for an intern or the beginning resident. It should be required reading once every six months for the resident in dermatology. The two chapters on specific lesions and extent, shape and distribution of these lesions are worth the price of the book.

—WILLIAM A. NEW Capt, MC USN

MEDICAL DEPARTMENT UNITED STATES ARMY Surgery World War II  
 Ophthalmology and Otolaryngology Edited by Chas. C. J. B. B. yd  
 C. J. B. B. yd MC USA Edited by Ophthalmology and Otolaryngology  
 M. D. Ed. f. r. Otolaryngology N. t. C. f. l. d. M. D. A. o. at  
 Ed. t. El. x. b. th. M. M. F. tridg. M. A. 605 p. g. ill. tr. t. d. H. c. l.  
 U. t. A. my. M. d. l. S. Off. of th. Surg. G. al. D. p. tm. t.  
 f. th. Army. W. h. gt. 25 D. C. 1957 For. l. by the S. p. d. t.  
 f. D. cum. t. U. S. G. v. m. t. P. t. ng. Off. W. h. ng. t. 25 D. C.  
 Pr. e. \$4

This volume of Surgery in World War II devoted to ophthalmology and otolaryngology is a comprehensive volume about both specialties during the war years. The book deals with the administrative aspects of ophthalmology and otolaryngology and the problems faced by the administrator during an emergency of such magnitude as the war.

In the chapters devoted to ophthalmology many of the problems peculiar to wartime practice are discussed. The civilian practitioner often with limited experience in the military was faced with problems of multiple intraocular foreign bodies, both malignant and nonmalignant eye diseases peculiar to tropical conditions, nutritional amblyopia, and blindness in service personnel.

One of the interesting features of the book is the history of development of the acrylic ocular prosthesis by the Dental Department. This contribution has been a big factor in our present day use of ocular prosthesis of this nature.

In the otolaryngology section of the book many of the problems of the otolaryngologist are discussed. Aside from the problems of administration there was the constant casualty rate from acute pharyngitis, tonsillitis, and otitis media. Deafness in the combat soldier was a common occurrence and much of the time of the otologist was devoted to audiometric studies and the rehabilitation of the deaf through lip reading and hearing aids. Some outstanding work was performed on facial nerve paralysis by decompression and autogenous nerve grafts. The chapter devoted to plastic surgery of the ear, eye, nose, and throat is especially interesting.

The book is well worth reading from a historical as well as professional standpoint by both civilian and military specialists. It will give the reader some idea of the multiple problem faced by the military specialist in the administration, treatment, and disposition of the war casualty.

—SHIRLEY A. FUHRING, Capt. MC, USN

THE YEAR BOOK OF OPHTHALMOLOGY (1957-1958 Year Book Series)  
 Edited by D. M. K. V. L. B. A. M. D. D. Oph. (O.) F. A. C. S.  
 F. R. C. S. (H.) 423 p. g. ill. tr. t. d. Th. Y. Book P. bl. h. s.  
 I. Ch. go. ill. 1958 P. e. \$7.50

This is the first Year Book devoted exclusively to ophthalmology. Previous volumes for more than fifty years have been combined year and ear, nose, and throat reviews. The separation into two volumes

has markedly benefited the ophthalmologic material and has permitted more complete discussions of articles in the literature. The comments of the editor at the conclusion of many of the abstracts contribute much to the value of the book. He gives not only the benefit of his own wide experience but frequently quotes other recent pertinent literature as well. This feature alone would be worth the price of the book. In addition this volume contains a 35 page lead article by Dr Irving Leopold on Recent Advances in Ocular Therapy. The book follows the same general topical outline as in previous editions. Desired material also is readily located through the use of separate indexes for subjects and authors. The book is not lavishly illustrated but it does contain photographs and diagrams when they are essential to ready comprehension of the abstracts. Literature of primarily research interest has not been included though this is being considered for future volumes.

Because of the extent of the literature which has been abstracted and the ease of quickly reviewing the latest information relating to a clinical condition this is an invaluable book for the busy practicing ophthalmologist. It is equally useful to other professional specialists in the consideration of eye involvement in general diseases. For these reasons it should be a required volume in medical libraries.

—VICTOR A. BYRNES *Brig Gen, USAF (MC)*

GENERAL PATHOLOGY based on Lectures delivered at the Sir William Dunn School of Pathology University of Oxford edited by Sir Howard Flor y 2d edition 932 pages illustrated W B Saunders Co Philadelphia P 1958 Price \$16

The title of this volume is somewhat misleading in that this binding houses a series of monographs on various aspects of pathology and related subjects rather than a complete discourse on the general aspects of pathology. These monographs are based on the lectures of Sir Howard and his associates and arranged as chapters in a logical sequence.

Subjects range from such standard titles as History and Inflammation to chapters on Some Biological Effects of Radiant Energy and Biological Factors in the Production of Antibodies. Each unit is treated in a learned fashion stressing pathologic physiology and avoiding the usual systematic descriptions of "dead house morphology." This approach coupled together with a comprehensive style results in a refreshingly different attack on standard material.

The paper print binding and illustrations are in keeping with the usual Saunders standards which combine ease of reading and durability. —BRUCE H SMITH J Cpt MC USA

## UNEXPECTED REACTIONS TO MODERN THERAPEUTICS—ANTIBIOTICS

by L. S. H. D. I. M. D. 146 p. g. Ch. r. l. C. Th. m. P. bl. h.  
Sp. g. f. Id. Ill. 1957 P. \$3

This book deals with severe reaction to antibiotics and quotes reports from the literature concerning such reactions. No attempt is made to estimate the frequency of occurrence but the author brings to mind the danger that exists in treatment by antibiotics. Because in a great many cases even with a careful history it was impossible to anticipate reactions some serious but infrequent reactions from any antibiotic must be expected. The first part of the book deals with reactions to major antibiotics penicillin with its skin reactions serious allergic reactions to infinitesimal doses and fatal anaphylactic shock streptomycin's toxic effects on the eighth nerve skin reactions and encephalopathy chloramphenicol's aplastic anemia gastrointestinal and psychic symptoms tetracyclines allergic reactions local mucosal changes with oral lozenges the staphylococcal enteritis which may follow. There is a short chapter on antibiotic-resistant bacteria showing the rapidity with which the staphylococcus becomes resistant. The remainder is devoted to less frequently used antibiotics neomycin erythromycin bacitracin fusidic acid nafcillin cycloserine and polymyxin all of which have the rather bad aspects. It is impossible to get an accurate estimate of the number of reactions to the drugs the reports are scattered and many reactions are not reported. This book would be a useful addition to a medical library.

—JAMES L. TOBIN C. I. USAF (MC)

## CEREBRAL LIPIDOSES A Symposium. Ch. m. L. B. g. r. M. D.

Ed. J. N. C. m. g. M. D. F. R. C. P. A. t. Edit. A. L.  
th. l. M. D. 212 p. g. 11 st. t. d. Ch. l. C. Th. m. P. bl. h.  
Sp. g. f. Id. Ill. 1957 P. \$8.50

According to the introduction by Doctor van Bogaert an attempt is made to classify the lipidoses of the nervous system including their relationship to the subgroup of demyelinating diseases known as leukodystrophy. Also another purpose is to check on the current value of histologic and histochemical methods in use in order to see if better procedures can be employed for more accurate information. Lastly an effort to compare various quantitative methods from different laboratories is to be a goal so that the cause of obvious discrepancies can be determined.

A considerable portion of the book is centered on histochemical technique for determining the chemistry of the lipids concerned purporting to give indications that leukodystrophy is a glycolipid which relates it to some of the primary lipidoses such as amaurotic idiocy. The whole question of myelin sheath formation is discussed from time to time.

One single classification of lipidoses offered in the book can be considered conclusive or final from a histologic or histochemical standpoint. L. Svennholm pleads for exercise of caution in drawing conclusions about the chemical substrate of disease from single

quantitative determinations or from mere histochemical studies. He believes that the problems of study in neuropathology must be approached on clinical, histopathologic and chemical grounds. In this book above the book does not provide a final answer to the classification of the lipidoses nor to their precise relationship to leukodystrophies but it does open further avenues of exploration. No doubt further clarification will be achieved by comparison of techniques but this is a commendable achievement. On the whole the book is rather erudite and esoteric. The book probably is best suited for those in neuropathology with a special interest in the lipidoses and their histochemistry.

—ARTHUR J. LEVENS Lt Col USAF (MC)

**CLINICAL AND IMMUNOLOGIC ASPECTS OF FUNGUS DISEASES** by Walter Wilson, M.D. American Lecture Series Publication No. 326 a Monograph in The Bannerstone Division of American Lectures in Dermatology edited by Arthur C. Curtis M.D. 280 pages Charles C. Thomas Publisher Springfield Ill. 1957 Price \$6.75

This interesting volume on fungous diseases should prove of great value to clinicians who are frequently perplexed by the variable manifestations of these diseases. The author relies heavily upon his own personal experiences with these diseases extending over a 25 year period, and his opinions and findings reflect his studious personal approach. The format of 22 chapters without charts, graphs or illustrations, is unique and novel. The initial seven chapters are devoted to a comprehensive consideration of coccidioidomycosis as a guide in the study of infectious diseases. In subsequent chapters the author repeatedly cites similarities or duplications of these phenomena in other mycotic diseases enabling the reader to obtain at least a logical explanation for heretofore obscure mechanisms. The work is not intended as an encyclopedic textbook but only as a supplement to the literature on certain aspects of fungous diseases. It is provocative, but easy reading and should as the author hopes stimulate others to a more exhaustive research and investigation in this field.

—CLAUDE B. WHITE Col USAF (MC)

**SPINAL ANESTHESIA** by John B. Dillon B.S., M.S., M.D. American Lecture Series Publication No. 326 A Monograph in American Lectures in Anesthesiology edited by John Adair M.D. 61 pages illustrated Charles C. Thomas Publisher Springfield Ill. 1958 Price \$3

This monograph of the author's method and technic in spinal anesthesia is very readable and can be digested leisurely in less than an hour. Consisting of 11 short chapters it offers a successful method of surgical analgesia in selected cases. Ten illustrations show such fundamentals as positioning the patient, distribution of the somatic nerves, contour of the spinal column and dosage chart. It is not designed as a work of reference and would be of little benefit to the qualified anesthesiologist. The author proposes its use by "the physician who performs spinal anesthesia but who has had neither the time nor the opportunity to explore some of its facets."

—ROBERT F. CORWIN Col USAF (MC)



## UNEXPECTED REACTIONS TO MODERN THERAPEUTICS—ANTIBIOTICS

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—JAMES L. TOBIN C I USAF (MC)

CEREBRAL LIPIDOSES A Symposium Ch r m n L B g n M D  
Ed J N C m g M D F R C P A s t Ed A L  
th l M D 212 p g Il t t d Ch l C Th m P b l h  
Sp g f Id Ill 1957 P \$8.50

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- GLAUCOMA** Transactions of the Second Conference December 3, 4, and 5, 1956 Princeton N J edited by *Frank W Hewell M D* 24 pages illustrated Sponsored by the Josiah Macy Jr Foundation, New York N Y 1958 Price \$4 95
- SYMPOSIUM ON RECENT CLINICAL ADVANCES—Pediatric Clinics of North America** May 1958 *Alan Ross M D* Consulting Editor 3,600 pages illustrated W B Saunders Co Philadelphia Pa 1958
- METHODS AND MATERIALS OF HEALTH EDUCATION** by *P Heston Schneider M S P H* Ed D 382 pages illustrated W B Saunders Co Philadelphia Pa 1958 Price \$5
- A MANUAL OF DENTAL ANESTHESIA** An Illustrated Guide for Student and Practitioner by *W Harry Archer B S M A D D S* 2d edition 115 pages illustrated W B Saunders Co Philadelphia, Pa, 1958 Price \$8 50
- LABORATORY MEDICINE HEMATOLOGY** by *John B Male M D* 72 pages 192 illustrations and 9 plates including 5 in color Black & Mosby Company St Louis Mo 1958 Price \$13 75
- RECONSTRUCTIVE AND REPARATIVE SURGERY**, by *Hans May M D*, F A C S 2d edition 1 115 pages with 1 030 illustrations, in color F A Davis Company Philadelphia Pa 1958
- MEDICAL EMERGENCIES** Diagnosis and Treatment By *Francis D Murphy M D F A C P* and Associate Authors Foreword by *Cecil H Mills Jr M D* 6th edition 635 pages illustrated F A Davis Company Philadelphia Pa 1958
- THE MEDICAL MANAGEMENT OF CANCER** by *Henry D Blau M D*, F A C P 179 pages illustrated Grune and Stratton Inc New York, N Y 1958 Price \$6 75
- ELECTRON MICROSCOPIC ATLAS OF NORMAL AND PATHOLOGIC HUMAN BLOOD** by *Frank N Low Ph D* and *James A Freeman* 347 pages illustrated The Blakiston Division McGraw-Hill Book Company, Inc, New York N Y 1958 Price \$25
- INTRODUCTION TO MEDICAL SCIENCE** by *Cullen H Muller M D*, M S, M P Dooby *E Dawes R N M A* 4th edition 600 pages illustrated W B Saunders Co Philadelphia Pa 1958 Price \$5 50
- THE CHEMISTRY AND CHEMOTHERAPY OF TUBERCULOSIS** A comprehensive and critical review of existing knowledge on the chemistry of tubercle bacilli and their products chemical changes and processes in the host, and chemical aspects of the treatment of tuberculosis by *Forrest H Long M D Ph D Sc D* 3d edition 450 pages illustrated The Williams & Wilkins Co Baltimore Md 1958 Price \$1
- HANDBOOK OF TREATMENT OF ACUTE POISONING** by *L H Herxhey M B E B A M D F A C P* and *G E Joron B A M D*, C M F A C P 2d edition 212 pages E & S Livingstone Ltd, Edinburgh and London 1958 The Williams & Wilkins Co Baltimore, Md exclusive U S agents Price \$4
- INTESTINAL OBSTRUCTION** by *Claude E Welch M D D Sc (Hon)* Illustrated by *Muriel McLatchie Miller* 376 pages The Year Book Publishers Inc Chicago Ill 1958 Price \$10 50
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## Monthly Message

Last year some members of the Medical Advisory Council of the Canadian Department of National Defence joined with the Civilian Advisory Council of this office and visited Maxwell and Gunter Air Force Bases and the Naval Air Training Station at Pensacola. The group consisted of Dr Joseph A MacFarlane Chairman of the Council and Dean of the University of Toronto Faculty of Medicine Dr Ian Macdonald Professor of Medicine at Toronto Brigadier Kenneth A Hunter RCAMC, the Executive Director of the Council and Air Commodore Alexander A G Corbet, RCAF.

This trip was so successful that in March 1958 the two groups joined again to visit Sandia Base and Holloman Air Force Base New Mexico and Edwards Air Force Base California. This time in addition to our own Council the group consisted of Dr MacFarlane Dr Alfred W Farmer Dr Desmond Magna and Air Commodore Corbet and a most cordial reception was accorded everywhere.

During these visits our guests sit with us at one of the regular meetings of our Advisory Council and our programs and problems are discussed together.

In the summer of 1957 on a trip to the Far Northeast a group of us while at Goose Bay took the liberty of visiting the Canadian Armed Forces Hospital on the other side of the airfield. At that time both the Director and Deputy Director were away the latter a surgical patient in the U S Air Force Hospital at Goose Bay. Nevertheless we received a most cordial reception from the lone medical officer still left on duty a 1957 graduate of Dalhousie University Faculty of Medicine at Halifax.

In September 1956 I was the guest of the Canadian Advisory Council at one of its meetings in Ottawa. A continuation of these mutually beneficial exchange visits is planned by both groups. During World War II in both the Mediterranean and the European Theatres we were closely associated first in England and then in Italy France and Germany and in 1950 a conference on medical supplies and standardization of equipment was held in Montreal including representatives from the United Kingdom.

Canada, and the United States, which I was privileged to attend. Unfortunately, little came of that meeting, but we hope that the exchange visits so recently inaugurated will continue with increasing success.

*Frank B. Berry*

FRANK B. BERRY, M. D.  
Assistant Secretary of Defense  
(Health and Medical)

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S g G l U t d St t A F

# UNITED STATES ARMED FORCES MEDICAL JOURNAL

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Volume IX

July 1958

Number 7

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## SEVERE DYSBARISM IN AIR FORCE OPERATIONS AND TRAINING

CHARLES A. BERRY *Major USAF (MC)*

THE term dysbarism is used to define the symptom complex resulting from exposing the body to reduced atmospheric pressure. It includes both trapped and evolved gas syndromes, and is distinctly separate from hypoxia. Decompression sickness is usually synonymous with severe dysbarism and neurocirculatory collapse.

The advent of jet aircraft with their altitude hungry engines has created a large population exposed to a significant decrease in atmospheric pressure in both the training and the operational situation. The number of persons exposed or potentially exposed to altitudes in excess of 30 000 feet will be further increased by the advent of all jet aircraft units in the U. S. Air Force and civilian jet airliners. Inevitably this increased exposure will lead to more cases of severe dysbarism.

### OPERATIONAL PROBLEM

The problem of severe dysbarism in operational aircraft has been highlighted in recent years by several deaths. Two cases in the U. S. Air Force have been reported by Haymaker, Johnston, and Downey<sup>1</sup> and mention was made of another. A fourth report has been received.<sup>2</sup> Fryer<sup>3</sup> described three deaths in the Royal Air Force occurring after aircraft flight and as a result of decompression sickness. In addition to these deaths there are numerous cases of severe dysbarism in persons who fortunately recovered.<sup>4-6</sup> The aviation medicine consultation service at

this school recently has studied two patients and received reports of six others all of whom suffered severe dysbarism in operational aircraft. One of these persons exhibits findings of a "permanent residual from his dysbarism episode. The pertinent data concerning these cases are summarized in table 1. There has been conflicting opinion concerning the possibility of permanent residual from decompression sickness. Some authors have stated the only known evidence was a dog with residual paralysis of the hind legs but this was prior to the report by Döbeln and Höök which described a chamber reactor with residual paralysis. In the U S Air Force case the patient shows damage of the left choroid and severe damage to the visual pathways manifested by bilaterally impaired color vision fields. This residual is called permanent on the basis that it existed from January 1953 to October 1954 when the patient was last seen. His present status is unknown.

TABLE Severe dysbarism during flight in U S Air Force 1953-5

Cs No.	D	Type of alt.	Clinical (ft)	Altitude	Clinical
	Feb 95	T 33	3 000 (dysbarism on)	0	left eye blurred, right eye normal
2	8 Feb 95	B 5	3 000	30	left eye blurred, right eye normal
3	20 Feb 1946	T 33	3 000	1 hr	left eye blurred, right eye normal
	25 Apr 1946	3	4 000	1 hr	left eye blurred, right eye normal
	Feb 95	3	30 000	15	left eye blurred, right eye normal
	5 Dec 95	4	3 000 (rapid decompression on)		left eye blurred, right eye normal
	Jul 95	T 3	3 000-32 000		left eye blurred, right eye normal
	95	B 79	35 000	3 in	left eye blurred, right eye normal

The eight cases of severe dysbarism in flight listed are not of great import when considered in the light of the hundreds of thousands of flying hours completed without incident in the same period. I believe however that many unreported cases exist and that the cost of an aircraft and the investment in a trained pilot make even one such incident a very undesirable and costly affair.

It is of interest to note that five of the eight reported incidents occurred in aircraft. Rapid or explosive decompression is of great concern in our high altitude high performance aircraft.

for it exposes the crew to reduced atmospheric pressure and at the same time increases the risk of hypoxia and dysbarism by its sudden onset. In a recent compilation of data on some 98 rapid decompressions in the U S Air Force occurring over a 52 month period there were no instances of decompression sickness noted. Only 32 of these decompressions occurred at altitudes in excess of 30 000 feet and of these only 8 were in bomber type aircraft. The fighters all descended rapidly and immediately, thus further reducing the risk of decompression sickness. Two cases listed in table 1 (cases 1 and 6) apparently were not reported to the Air Force Directorate of Flight Safety, but these men also had rapid decompression during this reporting period and they developed decompression sickness. In this regard it should be noted that frequently the T 33 is flown with the pressurization system functioning only well enough to lower the cabin altitude 1 000 or 2 000 feet below ambient. This is much more dangerous than rapid decompression for there is no emergency development of difficulty instead the insidious exposure to low atmospheric pressure exists during the entire flight plan.

Incidents of severe in flight dysbarism are not uniformly reported in the Air Force. The only sources of such information are cases reported in the literature by physiological training officers, flight surgeons or the aviation medicine consultation service. In order to gather more data on this subject this school has initiated proceedings to require reporting of these in flight or operational cases as we do the chamber reactors.

### TRAINING PROBLEM

In order to fly or even ride as a passenger in our high altitude high performance aircraft Air Force personnel must participate in a physiologic training course. The curriculum of this course includes an altitude chamber flight to 43,000 feet. A generally standardized flight pattern is used by the various training units. As a result of the large number of personnel exposed to altitude in this program a certain number of severe dysbarism cases (chamber reactors) are seen.

In the U S Air Force physiologic training program the various grades of chamber reactions are defined and reported as follows:

- Grade I—Any slight unnatural sensation
- Grade II—Slight to moderate pain not requiring removal from or interruption of the chamber flight
- Grade III—Moderate to severe pain or other reactions requiring removal from the chamber
- Grade IV—Any chamber reaction requiring admission to a hospital

In the Air Force during the years 1950 through 1955 there were 125 Grade IV chamber or dysbarism reactions reported.

The occurrence of the various symptom grades which precede the Grade IV reaction are tabulated for 51 580 trainees exposed to altitude in physiological training unit chambers during 1955 (table 2)

TABLE 2 Symptom by grade 51 580 men  
flight 1955 (men per 100 000 men flight)

Symptom	Grade			
	I	II	III	IV
Ep	6650	2437	514	
Abdominal pain	2738	1187	322	12
Head	1594	642	155	21
Sleep	1516	723	176	
Too high	285	142	118	
Choke	47	19		2
Cerebral symptoms				
durban	12	6	6	4
Other	432	167	178	54

The incidence figures calculated for Grade IV chamber reactors show an increase from 49 per 100 000 trainees in 1954 to 85 per 100 000 trainees in 1955 and to 110 per 100 000 trainees in 1956

A Record of Chamber Reactor is completed on each Grade IV reactor and copies forwarded to the Surgeon General and to the School of Aviation Medicine. These records were recently reviewed for a five year period (1950-1955) and the detailed findings reported.<sup>1</sup> The simple classification of these severe cases into chiefly circulatory, chiefly neurologic or mixed is one of several attempts at categorizing these reactions.<sup>14</sup> Review of the 195 records however revealed the following classification to be of value:

#### CLASSIFICATION

**Group 1** Persons having bends, chokes, gas, et cetera as an initial symptom followed by syncope or signs of impending syncope with recovery by the time ground level was reached or within a few minutes thereafter (Minor residual signs and symptoms such as mild pallor or sweating are not to be considered as significant provided the reactor is mentally alert and the blood pressure is normal.)

**Group 2** Persons having circulatory and other autonomic signs and symptoms at altitude who recover at ground level or during the two-hour observation period and then have a subsequent delayed reaction.

**Group 3** Persons having circulatory and other autonomic signs and symptoms at altitude which progress to immediate or delayed shock.

**Group 4** Persons having syncope without preceding symptoms

**Group 5** Persons with any of numerous neurologic signs and symptoms who either proceed to recovery or have residual defect (The pseudo paresis seen with severe bends must be carefully excluded from this group)

The number of reactors placed in each group is shown in table 3

TABLE 3 *Distribution of reaction groups in 125 Grade IV chamber reactors*

Reaction group	Number	Per cent
1	65	52.0
2	4	3.2
3	4	3.2
4	5	4.0
5	47	37.6
Total	125	100.0

The signs and symptoms of pallor, sweating, nausea and vomiting were considered to be of autonomic origin and were found associated with many of the reactions in different groups

Changes in blood pressure and pulse were thought to represent circulatory symptoms and signs. Neurologic signs and symptoms covered a wide range and included paresis, paralysis, scotomata and other visual field losses, convulsions, inconsistent and shifting reflexes, and involuntary urination or bowel movement

In comparing the findings on various factors analyzed, only groups 1 and 5 are used because the other three groups had so few cases

On first appraisal of the reactor records 22 cases were placed in group 4, but careful review of the narrative summary revealed other symptoms and signs noted prior to the loss of consciousness. The number was thus reduced to five cases in which the records showed all other signs and symptoms followed the loss of consciousness. I believe that careful observation of these five might have revealed other signs and symptoms and thus deleted group 4 in the classification

**Peak Altitude Attained and Rate of Ascent** Some reactions occurred on ascent and some on descent after peak altitude had been reached but in any case the highest altitude attained was always recorded. Some 77 per cent of group 1 and 79 per cent of group 5 had peak altitudes of 35,000 or 40,000 feet. The rate of ascent varied between 2,000 and 4,000 feet per minute in all cases except those occurring on rapid decompression

**Time Over 30 000 Feet** Some 50 to 60 per cent of groups 1 and 5 were exposed to altitudes in excess of 30 000 feet for less than 10 minutes. 90 to 97 per cent of both groups were over 30 000 feet for less than 20 minutes (fig. 1).

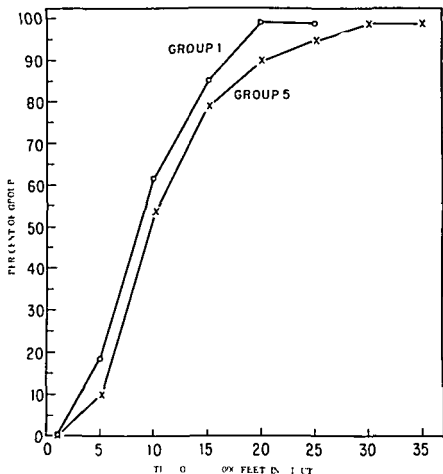


Fig. 1. Percentage of group 1 and 5 who died in excess of 30 000 feet for the indicated time.

**Body Type and Weight/Height Ratio** More than 80 per cent of the reactors were found to have a linear density (weight in pounds - height in inches) in the range 2.3 to 2.7. This is not unusual as our selection process gives us personnel in the mesomorphic category. Most of the deaths in U. S. Air Force aircraft have been in overweight nonflying personnel traveling in rear seat passenger status.

**First Symptom** 3 and 4 were the most frequently reported first symptom in all reaction groups except group 4 (the five cases

who had syncope without prior symptoms) The order of frequency for first symptoms in group 1 was bends, abdominal pain and dizziness while for group 5 it was bends, skin manifestations, and unconsciousness

**Signs and Symptoms in Chamber** Loss of consciousness was the most frequent symptom in groups 1 4 and 5 Dizziness was second in group 1 In group 5, there were three other symptoms that tied for first place with unconsciousness these were paralysis or paresis, abnormal vision and dizziness A high percentage of all reaction groups had bends (table 4) Chokes occurred in all groups except group 4 Abdominal distension was twice as high (33.8 per cent) in group 1 as in group 5 (19.1 per cent)

TABLE 4 *Per cent distribution of symptoms reported in the chamber in 125 Grade IV chamber reactors 1950-1955*

Symptoms in chamber	Group				
	1	2	3	4	5
Bends	35.4	25.0	75.0		55.3
Choke	7.7	50.0	25.0		10.6
Abdominal distension	33.8	25.0			19.1
Skin reaction	4.6	75.0			23.4
Apprehension	27.7	25.0	25.0	40.0	40.4
Pallor	16.9		25.0	40.0	6.4
Sweating	30.8	50.0	25.0		42.6
Nausea	16.9		50.0	20.0	6.4
Vomiting	16.9				19.1
Cyanosis	23.1		25.0	60.0	19.1
Dizziness	55.4	25.0	100.0	60.0	61.7
Hyperventilation	30.8	25.0	25.0	20.0	34.0
Spasm and convulsions	13.9			20.0	21.3
Headache	9.2				14.9
Abnormal vision	12.3	25.0	75.0		61.7
Paralysis or paresis					61.7
Loss of consciousness	58.5	50.0	75.0	100.0	61.7

Skin reactions occurred in only 4.6 per cent of group 1 while they occurred in 75 per cent of group 2 and 23.4 per cent of group 5. Comparisons between groups 1 and 5 are shown in figure 2.

**Days in Hospital** Of the group 1 cases 87 per cent were hospitalized only two days or less. Of the group 5 cases, 49 per cent were hospitalized only two days or less, 42 per cent were hospitalized from three to seven days, and 9 per cent for 10 to 17 days.

**Treatment** Only 35 per cent of group 1 reactors received treatment of oxygen and/or fluids while 58 per cent of the 45 group 5 reactors received either oxygen, fluids, or both.



The only death in the 125 reactors was reported in detail by Adler. One other death was removed from the data as it was due to explosive decompression and lung rupture. Thus some 124 reactors recovered. The questions as to the number who have a residual and the number who are still flying must remain unanswered for the present. Denitrogenation was limited to the time of the flight in most all instances.

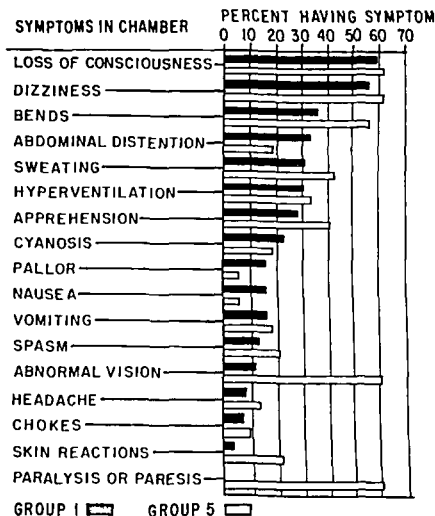


Fig. 2. Percent with symptoms with hypobaric oxygen in the chamber. Group 1 and 47 Group 5. Data from U.S. Armed Forces Medical Journal, 1950-1955.

### DISCUSSION

Loss of consciousness was the most frequently recorded symptom in three of the five reactor groups. In most instances

it was preceded by moderate to severe symptoms of dysbarism such as bends, chokes, abdominal distension and/or skin reactions. The mechanism of this loss of consciousness remains an interesting enigma. The cause of the loss of consciousness in these cases can only be speculated on and some form of vasovagal reaction seems a probable choice. A respiratory reflex action is possible. I believe that many if not most of the type 1 reactions are the result of vasodepressor and vasovagal reactions and thus explainable.

The basis of loss of consciousness in the neurologic reactions is unknown. Speculation as to its cause may lead to a reflex mechanism as discussed above but further information is sorely needed. It is of interest that loss of consciousness was reported only in the in flight reactors who died.

The reluctance to return to flying status those individuals having an episode of unexplained loss of consciousness and our inability to describe what is an acceptable stress for causing fainting (syncope) in a "normal" person, leave the disposition of such reactors as a pressing but unanswered problem.

The exposure period need not be long to produce a severe dysbarism reaction. The large percentage of reactors (90 to 97 per cent) have less than 20 minutes over 30 000 feet. This finding may be of some importance in developing safety procedures for future civilian jet airliners flying with unselected passengers.

Severe skin reactions such as rash and mottling were almost four times as frequent in the group 5 cases as in the group 1 cases. Thus skin reactions are more often associated with neurologic lesions and should be regarded as a premonitory sign of rather serious importance. A recent report by Rait<sup>13</sup> puts great emphasis on a fatty liver and fat emboli as the etiologic agents in these cases. Petechiae of the skin have not been reported in these cases.

The disposition of cases of decompression sickness continues to be a problem in our aviation medicine consultant centers. Although each case is evaluated individually the huge majority of decompression sickness cases have not been returned to flying status for in our service this implies unlimited flying status. This usual reluctance to return such cases to flying is based on the probability that such an individual is more likely to have a similar episode if again exposed to altitude. Evidence to support this probability was reported by Romano and associates.<sup>14</sup>

Two Air Force patients<sup>15, 16</sup> were returned to flying status and the outcome and their present status is unknown. The patient reported on by Rait was also returned to flying and exposed to altitude in the low pressure chamber (37 000 feet) without recurrence of his difficulty.

It would seem that there are two questions to be answered before we can consider returning such individuals to flying status and thus exposing them to the stressful environment which produced their symptoms

1 Does the patient have any neurologic residual?

2 Is the risk of exposing these individuals to altitudes in excess of 30 000 feet greater than that encountered in exposing persons who have never had an episode of decompression sickness?

In order to answer these questions adequately we must gather more information There has been no follow up program for decompression sickness cases in the Air Force A project is being initiated to secure the return of the 195 reactors reported in 1950 1955 and the 48 reactors reported in 1956 to this school for a follow up evaluation This program will include the known in flight cases and particularly those who have been returned to flying status It is proposed to use every means at our disposal to determine the presence of any residual defect or greater predisposition As a step to assist in evaluation of future reactors the Record of Chamber Reaction has been modified to provide more information

Even with some increase in numbers the total number of reactors compared to the persons trained in the U S Air Force is small The British (Royal Air Force) have been concerned by the risk of such training and therefore have modified their training to render it less stressful Whittingham<sup>7</sup> reported a similar cessation of training for civil airline (British Overseas Airways Corporation) crews I believe the value of the physiologic training program in preventing even more in flight incidents of hypoxia disorientation dysbarism et cetera far outweighs any risk so far encountered

At the present time what can we do about the treatment and prevention of neurocirculatory collapse at altitude? Due to our lack of knowledge only prophylaxis and improved symptomatic treatment is available On the basis of our present knowledge it would seem wise to attend to the following

1 Indoctrinate physiological training officers and chamber observers in early recognition of symptoms and signs of dysbarism

2 Return to ground level any person with a sign or symptom suggestive of severe dysbarism This applies to persons in operational aircraft as well as in low pressure chambers Trainees with any symptom of dysbarism should not be used as hypoxia demonstrators

3 Severe skin reactions deserve particular attention and trainees with such reactions should be recompressed immediately Ordinarily such cases have other symptoms or signs which would require their return to ground level

4 Prevention of obese people from taking altitude indoctrination. These people can be eliminated by the flight surgeon on his pretraining physical examination.

5 Continue the conservative treatment policy and hospitalize all chamber and altitude reactors except those with minor bends, gas, sinus pain, earache, or toothache.

6 Consider the temporary use of Levophed (brand of 1 nor epinephrine) or Aramine (brand of metaraminol bitartrate) in the recovery room in the event the blood pressure is very low or unobtainable.

7 Initiate dextran or intravenous fluid therapy as rapidly as possible in order to have a vein open in case shock develops rapidly.

8 Use a gas mixture of 95 per cent oxygen and 5 per cent carbon dioxide for treatment of all severe reactions. Carbon dioxide has been shown to be a potent cerebral vasodilator and such action is needed in these cases.

9 Further investigation of recompression to greater than atmospheric pressure (plus 2 atmospheres) as a treatment measure as advocated by Behnke.<sup>16</sup> Availability of a chamber capable of doing this has been a problem in Air Force facilities, but the new School of Aviation Medicine chambers will have this capability.

10 Spinal tap should be strongly considered as a diagnostic procedure in all reactors with neurologic signs or symptoms. Some have advocated spinal puncture and removal of from 5 to 10 ml of fluid as a therapeutic measure,<sup>1</sup> but evidence in this area is equivocal. In practically all instances where a spinal tap was performed, the pressure and laboratory findings were normal. An exception was one of the in flight deaths where an initial diagnosis of cerebral hemorrhage was made bolstered by a spinal fluid pressure of 260 mm of water and the presence of 20 red blood cells per  $\mu$ l. In spite of the usually normal findings improvement in the patient has been reported. However many if not most cases have recovered without spinal puncture.

### SUMMARY

An increased exposure of Air Force personnel to altitudes in excess of 30,000 feet has led to more reported cases of decompression sickness in both operational aircraft and low pressure chambers. Fight Air Force in flight (operational) reactors who survived have been reported in addition to four deaths. A plan for reporting of these cases has been initiated. During the period 1950-1955, there were 125 Grade IV dysbarism reactions reported in the Air Force. These reactions were classified into five groups which could briefly be characterized as (1) circulatory reactions following bends et cetera with recovery at ground level or within two hours afterward, (2) circulatory reactions with recovery and then delayed reaction, (3) circulatory

reactions progressing to shock (4) initial syncope without previous symptoms and (5) neurologic signs and symptoms

Of the reactors 90 to 97 per cent were above 30 000 feet for less than 20 minutes and 50 to 60 per cent for less than 10 minutes. Bends was the most frequently reported first symptom. Loss of consciousness was the most frequent symptom reported during the altitude exposure. Skin reactions were most frequently associated with delayed (group 2) and neurologic (group 5) reactions. Some suggestions are made for further study of the problem and for treatment of the reactors.

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# LIMITED THORACOTOMY AND ENZYMATIC THERAPY IN THE TREATMENT OF EARLY CLOTTED HEMOTHORAX

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THE medical literature on treatment of the patient with hemothorax is legion. In the days before the development of thoracic surgery, a clotted hemothorax committed a patient to the life of a pulmonary cripple with all the future complications of a fibrothorax. Surgeons have learned much from experience gained in World War II about the treatment of this condition so that at the present time therapy has become fairly well standardized.

Ideally, the treatment of hemothorax from any cause is the early, continued and complete removal of blood and air from the pleural cavity. Whether this is accomplished by needle aspiration, intercostal catheter drainage, or rarely, thoracotomy if indicated, is a matter of conjecture and depends on the preference of the surgeon. However, there will be patients where the most diligent pursuit of this objective fails and who remain with a clotted hemothorax. It is this type of patient—the one with an early clotted hemothorax—with which this article is concerned.

Enzymatic therapy (streptokinase and streptodornase) in hemothorax and empyema has been advocated by Sherry, Tillett and Read.<sup>1</sup> Others have reported encouraging results with these enzymes.<sup>2-5</sup> On the other hand, some question the use of enzymatic therapy. It is our belief that when enzymatic therapy is applied to the selected case *to wit*, an *early* clotted hemothorax, that much benefit may be gained in conjunction with other forms of therapy.

Decortication of an encapsulated lung due to clotted hemothorax or organized empyema is now an accepted surgical procedure. Much is owed to Samson and Burford and Tuttle, Langston and Crowley for their work in developing this procedure during and after World War II. The optimum time to perform this procedure has been stated to be about three weeks after the

occurrence of the hemothorax and indeed if performed at this time is a simple and safe procedure. In the borderline case however where there is a question of whether decortication is really indicated or not too often the decision is to wait two or three months and further evaluate the patient. In military life as well as civilian the implications of such a decision are clear. In either case the result is no gainful work during the observation period or at best work of a limited nature.

Within 10 days after the onset of a hemothorax it usually will become apparent to the attending physician whether or not he will be successful in evacuating all blood from the pleural cavity. The number of chest aspirations required, the success of such aspirations, clotting tendency of the blood removed, radiographic appearance of the chest, examination of the patient et cetera will aid in arriving at an early decision. Once it has been determined that further aspiration of the chest, whether by needle or intercostal catheter drainage is futile and if any significant degree of hemothorax remains we have adopted the following plan of therapy. A limited thoracotomy is performed resecting about 4 to 5 inches of the 6th or 7th rib laterally with the patient in the standard thoracotomy position. The pleural cavity is opened and all soft clots are removed. Pockets of encapsulated blood are broken up and fluid is removed by suction. At this stage of the disease any fibrinous deposits on the lung are very loose and lend themselves to easy removal. A lighted retractor within the chest cavity is very helpful and provides adequate illumination. No effort is made to do a complete decortication—only the clots and fluid are removed, pockets broken up and loose filmy exudates over the lung surfaces are removed. A large right-angled No. 45 French intercostal catheter is then inserted in the lowermost portion of the chest in the midaxillary line with the intrapleural end of the tube pointing posteriorly. This is then connected to a water trap.

Immediately following the operation 2 ampules of Varidase (brand of streptokinase streptodornase) totaling 200 000 units of streptokinase and 50 000 units of streptodornase are mixed in 20 ml of physiologic saline solution and inserted into the pleural cavity through the chest tube which has been clamped. Instructions are given the nurse to leave the tube clamped for 12 hours and then to release it. If during the 12 hour period the patient's temperature rises to 104 F the tube is immediately unclamped. This procedure can be repeated daily if indicated by lack of clearing on the daily chest roentgenogram. Usually only two injections of enzymes are required.

Although our experience with limited thoracotomy, limited decortication and subsequent enzymatic débridement of the pleural cavity covers only a few cases the results achieved have been excellent and we believe warrant reporting.

## CASE REPORTS

Case 1 A 26-year-old Caucasian in March 1957 suffered a right spontaneous pneumothorax for which he was successfully treated at another hospital. On 25 July he developed a spontaneous right hemothorax, was admitted to another hospital and then transferred to this hospital two days later. Needle aspiration of the right side of the chest on the day of admission resulted in removal of 350 ml of blood. A roentgenogram showed very little change following aspiration. The following day 225 ml of thick blood which clotted in the needle and syringe were removed. Aspirations were performed daily thereafter without success (fig 1). On 2 August 1957 eight days after the onset of the spontaneous hemothorax a "limited" right thoracotomy was performed removing about 5 inches of the midportion of the 6th rib.

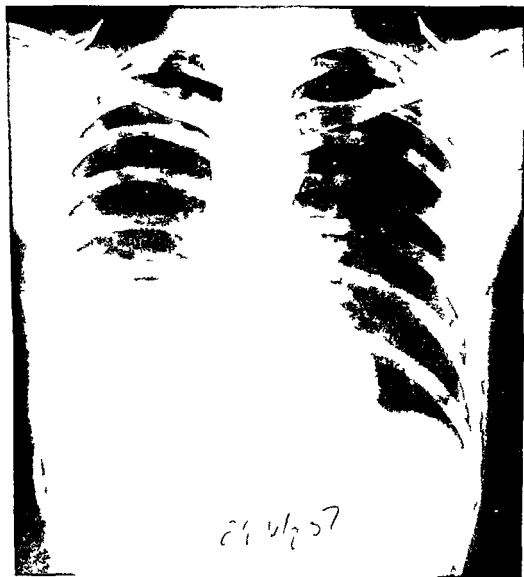


Figure 1 (case 1) Postoperative roentgenogram of chest showing clotted hemothorax



All clots were removed fluid was aspirated by suction and some loose fibrinous exudate was removed from the lung surface. A No. 45 French right angled chest catheter was placed in the 9th interspace in the midaxillary line and connected to a water trap. That afternoon 200 000 units of streptokinase and 50 000 units of streptodornase were placed in the pleural cavity through the chest tube and the tube clamped. The patient was then turned every half hour to ensure adequate distribution of the enzymes within the chest. Two hours following this the patient's temperature rose to 102.6 F the highest attained. Twelve hours after institution the chest tube was unclamped and about 1 000 ml of bloody serosanguineous material collected in the water trap. This procedure was repeated the following day and upon releasing the clamp from the chest tube only 100 ml

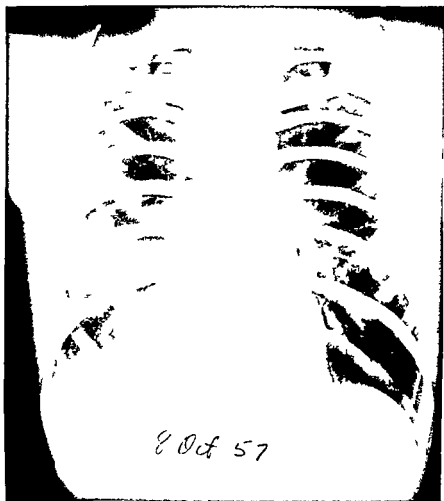


Fig. 2 (1) The roentgenogram demonstrates the condition of the lungs two months after limited thoracotomy and enzymic therapy.

of fluid drained into the bottle. The chest tube was removed the following day and convalescence thereafter was uneventful. The patient was sent on convalescent leave 11 days following thoracotomy. A follow-up roentgenogram (fig. 2) on 8 October revealed very satisfactory resolution of the hemothorax and complete lung expansion.

**Case 2** A 26 year-old man was admitted to this hospital on 13 May 1957 three hours after an automobile accident in which he suffered multiple abrasions and contusions and a fracture of the 10th rib on the left plus a compression fracture of the 10th dorsal vertebra. The admission chest film showed a minimal left hemopneumothorax. Follow up roentgenograms on 23 May 1957 showed a delayed massive hemothorax. A tap done at this time produced 1 550 ml of dark red blood.



Fig. 3 (case 2) Preoperative roentgenogram showing multiple fluid level

which clotted immediately on standing. A repeat tap the next day produced only 440 ml of blood which also clotted immediately on standing. Further taps during the next two days produced little if any blood and it was believed that the patient had a clotted hemothorax (fig 3). A limited thoracotomy was performed on 27 May. At this time the lung was noted to be encased in semifibrous peel and could not be fully expanded. Multiple pockets of clotted and unclotted blood were removed by breaking up the loculations and aspirating the blood and debris (1 225 ml). A No. 45 French chest tube was placed in the chest and connected to a water trap. The next day 200 000 units of streptokinase and 50 000 units of streptodornase were injected through the thoracotomy tube into the chest. The tube was clamped and opened



Fig 4 (a 2) Postoperative film.

after 12 hours. The highest temperature elevation was 102°F. Upon unclamping the tube 1 500 ml of bloody serous fluid was expelled into the water seal drainage bottle. The next day another similar dose of the enzymes was injected and when unclamped after 12 hours 1 000 ml of fluid was obtained. The tube was removed the following day and from then on the patient made an uneventful recovery (fig. 4).

### DISCUSSION

There will be some surgeons who upon reading this paper will raise the question of "why a limited thoracotomy?" "Why not perform a standard thoracotomy and finish the job then and there?" The answer to these questions is that if some type of operation is to be performed, a "limited" thoracotomy has the advantage of less operative trauma, less reluctance on the part of the surgeon to operate in a borderline case, and fewer postoperative complications such as chest pain, failure to cough, and atelectasis. Convalescence is rapid and uneventful. Hospital stay is definitely shorter following "limited" thoracotomy.

It is emphasized again that the regimen outlined here is for a very select group indeed, and is not advocated for late cases of clotted hemothorax or organized fibrothorax or empyema. If it is ascertained at limited thoracotomy that a more formal operation is indicated by the findings within the chest (thick dense, adherent exudate over the lungs, diaphragm, mediastinal pleura et cetera) it is a simple matter to extend the incision to that of a standard posterolateral thoracotomy size and carry out a formal decortication.

### SUMMARY AND CONCLUSIONS

"Limited" thoracotomy and "limited" decortication in conjunction with enzyme therapy is proposed as another form of treatment in *early* clotted hemothorax (8-12 days after onset). Indications that open thoracotomy will be required for clotted hemothorax usually become manifest 8-10 days after the onset of hemothorax. A plea for earlier operation is made. Early operative intervention results in a technically easier procedure with resulting better lung function for the patient. Early "limited" thoracotomy and decortication along with enzyme therapy has achieved excellent results in a small series of patients; has resulted in fewer days in the hospital and a much lower morbidity rate.

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### THE PHYSICIAN'S MOST PRECIOUS POSSESSION

Ordinarily nowadays most patients can be told their diagnosis as soon as it is made. If it is cancer the one is probably therapy available to cure it or at least to control it for a while. Radical surgery and radical irradiation are so severe—give the patient so much discomfort, risk his life so much, and carry so much in the way of both the sequelae—that one can not expect an intelligent patient to accept them without proper reason. But the diagnosis should not be given until it is certain, or at least as certain as one can make it. A doctor needs a vivid appreciation of the emotional turmoil that he inflicts on his patient with a diagnosis of cancer. If the diagnosis is withdrawn the sense of relief is lovely, but it does not recompense the patient for what in his mind he has already suffered. If the doctor tells his patient that the tumor is benign and then later has to explain that it is cancer in order to get him to submit to the necessary operation, the doctor can lose the patient's confidence. His trust in his physician is one of the patient's most precious possessions. I am not talking about the fact that it is the physician's most precious possession too, or that it is amazing how so many ordinary persons can have such trust grow up between them. What I wish to emphasize is that this trust must not be compromised.

—R. R. NEWELL, M.D.  
*J. Chron. Dis.*  
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# PRIMARY SPLIT SKIN GRAFTING FOR TREATMENT OF LARGE PILONIDAL CYSTS

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**A** PROBLEM of considerable importance in the military service is the treatment of pilonidal disease Buie and Curtiss<sup>1</sup> stated that 78,924 patients with this disease were admitted to Army hospitals between 1941 and 1945 Similarly, in the Navy 630 701 man days were lost and 7 409 operations were performed between 1944 and 1951 because of pilonidal disease The high incidence in the younger age group is well established

The length of time necessary for healing varies according to the type population being treated In military hospitals, it necessarily is prolonged because the patients usually are retained on the "sick list" until they are fit for full duty, in most instances this means until the wound is completely healed Experience has shown that if these men are returned to duty before complete healing takes place, additional man days are lost because of the higher incidence of recurrence

The reported "healing time" for the different operative procedures varies according to the prejudices of the authors and their particular technic Swinton and Markee<sup>2</sup> reported a healing time of 3 to 8 weeks in a group of 6,625 cases where only excision of the pilonidal cyst was done Berkowitz<sup>3</sup> listed the average healing time required for various methods of treatment as follows open packing, 86 days partial closure, 55 2 days, and primary closure, 30 6 days

Weeks and Young<sup>4</sup> reported an average hospitalization of 52 days with the open method of treatment and 33 days using the closed method Palumbo, Larimore, and Katz,<sup>5</sup> reporting on 171 cases, gave the average period of hospitalization for the open method as 17 2 days, for primary closure as 22 4 days, and for marsupialization as 16 9 days No mention or reference was made to the actual healing time or days lost from work

An additional factor in this disease, which accounts for the excessive number of man days lost, is the high incidence of

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recurrence Probably as indicated by Swinton and Markee one of the most frequent causes of recurrence is improper aftercare of the wound Turell stated The tendency to recurrence following any operation characterizes this lesion It is now almost universally realized that recurrence following an operative procedure is seldom due to overlooked remaining pilonidal sinuses but is often the result of the incomplete obliteration of dead space which has become infected

The high recurrence rate following primary closure of a pilonidal cyst is well established Palumbo, Larimore and Katz reported an over all recurrence rate of 21.9 per cent in a series of 1165 cases reviewed in the literature where primary closure was used The incidence of recurrence is high with other procedures as well Swinton and Markee reporting on the results with 123 patients treated between 1946 and 1952 at the Lahey Clinic Boston Mass showed an 18 per cent recurrence rate with excision only 6.6 per cent with marsupialization 32 per cent with excision and simple primary closure and 19 per cent with excision and primary closure using a modified Pope technic Kleiman had an over all recurrence rate of 16.2 per cent in a group of 481 patients treated by various methods In another group of 118 patients reported by Kleitsch and Cherry there was a 9.3 per cent recurrence rate Dwight and Maloy reported an average recurrence rate of 11 per cent in 411 cases followed for a year or more As shown in table 1 the rate varied from 6 to 18 per cent depending on the operative procedure employed

TABLE 1 P t / r r p t t / l l w d f  
y m /t n p t / p l d l

Typ	f Op	t	C ( mb )	R (p t)
E	and mpl l ur		24	8
E	and part l l ur		17	6
E	and gl t l fl p l ur		159	18
E	and w l ur		48	12
E	on and p k l g		75	12
I	and p k ng ( b )		40	7
I	o and p k ng		48	12

In an attempt to improve on these results I employed a method that had the advantages both of wide excision as used in the block excision and of primary closure This was accomplished by use of a primary split graft applied to the wound after a block excision had been performed Neither the method nor the basic technic are new or original and although only a few cases treated in this way appear in the literature it is provable

that this method has been long used but little reported.<sup>11</sup> Boger and Pinkham<sup>12</sup> presented the largest series, a group of 25 patients. They had an average postoperative hospital stay of 28.2 days, the longest stay being that of a patient in whom an additional cyst was found later and was not treated by skin graft. The recurrence rate in this series was not given.

### METHOD AND TECHNIC

The technic used is simple and effective as long as one adheres to sound surgical principles. Grafts are applied only to tissue free of inflammatory changes. To ensure this, the patients are placed on sitz baths and antibiotics several days prior to operation. If the cyst is not draining freely or is fluctuant, the sinus tract is opened by sharp incision and packed open with iodoform gauze for 24 hours. The patients are placed on a liquid diet 24 hours prior to surgery, and the lower bowel is thoroughly cleansed with repeated tap water enemas.

The operation is performed under spinal anesthesia. To prevent contamination of the donor site, the split graft is taken prior to probing and excision of the pilonidal cyst. The posterior surface of either the right or left thigh is used. The graft is taken with a Barker Vacuotome\* (fig. 1). The donor site is covered with fine mesh silk and a sterile pressure dressing applied. Care is taken to apply pressure from the toes to above the upper limits of the donor site to prevent edema distal to the dressing.

Following application of the dressing, the sinus tracts are probed circumferentially to determine the approximate size of the cyst and its ramifications (fig. 2). A wide excision of the cyst or sinus tracts down to the sacrococcygeal fascia is done, taking care not to enter the cyst or sinus cavity at any point. Particular care is taken to secure hemostasis.

The graft is applied to the pilonidal wound, anchoring it with a continuous No. 00000 plain catgut suture running in a vertical manner in the midline and extending parallel rows of suture material at 1 cm intervals, from the midline. The graft is anchored circumferentially to the wound edges with a continuous locked suture of the same material. A Stent type of dressing using a foam rubber form is anchored in place with circumferentially placed No. 20 black silk sutures. Additional relaxation of the grafted area is obtained by placing a pressure dressing over the Stent dressing, using fluffed gauze and long adhesive strips.

Postoperatively the patient is placed on antibiotics and bed rest for five days. He is given a liquid diet supplemented with a high vitamin intake especially ascorbic acid. Bowel movements are discouraged by the use of paregoric. On the first post



A minimum of two changes of dressings per day is required. We have found that the use of sitz baths has not been detrimental to grafted skin that has taken if started after the sixth postoperative day. We use them earlier if there are any signs of infection or inflammation. The donor site dressing is removed between the 10th and 14th postoperative days and the patient is returned to duty as soon as the wound has completely epithelialized.

## RESULTS

In an attempt to correlate the results of this method with those of other methods, two groups of patients were selected at random during the period of 1950 to 1956. One group of 50 patients were treated by marsupialization or block excision and a second group of 49 were treated by block excision and primary split skin graft.

In the first group the average number of hospital days necessary for complete healing was 66.14. The average postoperative hospital period was 59.34 days. No attempt was made to determine the recurrence rate in this group because this figure has been previously documented by many other writers. In the second group the average number of hospital days necessary for complete healing was 32.65. The average postoperative period for this group was 25.82 days.

Of the 49 patients treated in this manner, 39 were followed either by physical examination or questionnaire for from 6 months to 5 years. Of these 39 patients, 5 complained of slight drainage at the operative site requiring follow up treatment on an outpatient status. Only 1 of the 39 (2.6 per cent) required further hospitalization. He had a block excision of a pilonidal cyst and a primary split skin graft on 27 May 1950. The postoperative healing time was 19 days and he required a total of 26 days hospitalization before he could be returned to full duty. He returned to the hospital in 6 months with a diagnosis of ischioanal abscess. Proctoscopy did not reveal an internal sinus tract. The abscess was incised and drained. When inflammation subsided, probing of the cavity revealed a tract that ran up to the lower border of the previously grafted site. In this case recurrence resulted from incomplete excision of the pilonidal sinus at the time of the original procedure.

It is believed that the postoperative convalescence and hospitalization have been materially reduced using this method and follow up studies indicate a lower recurrence rate. The procedure has its disadvantages in that the preoperative preparation, the operation and postoperative care are more time consuming than they ordinarily are in block excision or marsupialization. Other disadvantages pointed out by previous writers have not been borne out in this series. Turell stated

that grafted skin in the sacrococcygeal area cannot withstand the strain incident to full military physical duty status or corresponding stress and strain in civilian pursuits. He believed that grafted skin is easily affected by slight trauma.

In this series all patients with split grafts were sent back to full duty at the average time indicated (25.82 days). Except for the one recurrence, there has been no indication over the past five years that the grafted areas have not withstood the rigors of active military duty. Indeed, one of the patients, following the split graft procedure, did duty in Korea during the Korean Conflict and was awarded the Legion of Merit for outstanding services. He has been followed for five years without a recurrence and has no complaints referable to either the donor or recipient sites.

This series also bears out an observation made by Hubly, Mustard, and Stiefel<sup>11</sup> that, although the graft is sutured directly down upon the sacrococcygeal ligament, no patient has complained of pain or discomfort in that area. Another criticism of this method has been that grafts applied to fresh wounds leave large defects. This has not been a problem because, as Hubly and associates pointed out, the original operative defect is lessened by some 30 per cent to 50 per cent as a result of contraction. Furthermore, experience in this series indicates that the greater the tension placed on the graft at the time of its application, the greater will be the degree of subsequent contraction.

Some authors<sup>10</sup> propose a delayed skin grafting procedure, applying the graft after clean granulations have formed. It is thought that such a delay is not necessary if strict attention is paid to sterile precautions. There has been no difficulty with irregularly surfaced or cosmetically unsatisfactory grafts. An additional one to two weeks of hospitalization is added if one waits for clean granulations to appear before grafting.

Thus far there has been no cause for regret in employing the primary split graft procedure in the treatment of pilonidal disease. The results are encouraging enough to allow this procedure to be employed as one of the routine methods for treating large pilonidal cysts where convalescence would be unduly prolonged with one of the accepted procedures for the "open method" of treatment.

#### SUMMARY

The prolonged hospitalization and convalescence usually necessary for the treatment of pilonidal disease are of particular concern to the armed services. To meet this problem, a method of treatment by block excision followed by primary skin grafting is proposed.

The encouraging results obtained in 49 cases su  
this method is advantageous for the treatment of large  
cysts where convalescence would be unduly prolonged  
of the accepted procedures used in the open method  
ment

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# A SHIGELLA LIKE INTERMEDIATE SEROTYPE ALKALESCENS DISPAR 01 var KOJI

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**D**URING the course of a dysentery epidemic among impounded prisoners of war in the summer of 1951,<sup>1</sup> several thousand cultures were submitted to this laboratory by the Dysentery Research Unit. The majority of these were members of the genus *Shigella*, notably of the Flexner group and occasionally *Salmonella* sp.<sup>2,3</sup> On routine examination in this laboratory, a group of apparently related, aberrant strains was encountered and subjected to further study.

It was found that these organisms were capable of producing only acid when cultured in broth containing glucose, trehalose, maltose, arabinose, xylose, or sorbitol. Those which were not fermented after 15 days' incubation were sucrose, lactose, raffinose, rhamnose, mannitol, dulcitol, inositol, dextrin, glycerol, adonitol and salicin. The organisms were nonmotile, formed indole, did not produce H<sub>2</sub>S, and were unable to utilize citrate (Simmons Citrate Agar) as a sole source of carbon. The test for trimethylamine oxide reduction<sup>4</sup> was negative, the methyl red test was positive, acetylmethylcarbinol was not produced, and nitrate was reduced. The organisms grew at 45.5°C.<sup>5</sup> The KCN and ninhydrin tests were negative and urea was not split.

These reactions are consistent with those expected of members of the genus *Shigella*; however, in the slide agglutination tests using cell suspensions<sup>6</sup> there were no reactions. Therefore, a species of *Shigella* may possess thermolabile blocking substances, the suspensions were heated to boiling. The heated antigens reacted with the Flexner group serum but with none of the specific sera of this group. *Alkalescens Dispar* 01 (A D 01) serum caused marked agglutination by slide test, and slight reactions in serum against *Shigella dysenteriae* 1 were observed.

Although these organisms reacted in both *S. dysenteriae* 1 antiserum and in A D 01 serum, the biochemical reactions are consistent with neither of those species—xylose was fermented, indole was formed and the organisms grew at 45.5°C, of which

<sup>1</sup> F m 406th M d c l G I L b r t o r y APO 343 Sa Fr crisc Calif Lt J ffries  
w i t h D p a r t m e n t B i o t e c h n o l o g y U n i v e r s i t y T e n n e s s e e K n o x v i l l e T e n n

the *Shiga* bacillus is incapable but which is characteristic of A D 01. On the other hand mannitol was not fermented, trimethylamine oxide was not reduced, the KCN and ninhydrin tests were negative which is inconsistent with A D 01 but not with *S. dysenteriae* 1.

Thus this group of organisms of which strains 891, 2499 and 3162 were representative did not correspond in its antigenic structure and biochemical reactions to any of the known members of the genus *Shigella*. It became apparent that there should be further investigation with respect to the antigenic make-up of the group.

### MATERIALS AND METHODS

**Antigens.** The antigens used for the production of antiserum were prepared by inoculating tryptose phosphate agar slants and incubating at 37 C for 24 hours. The growth was suspended in physiologic saline solution containing 0.3 per cent formalin and filtered through glass wool. The filtrate was held at 37 C overnight and centrifuged; the cells were washed once in formalinized saline and resuspended. The final suspension was adjusted to a density corresponding to the No. 3 McFarland nephelometer (about  $9 \times 10^8$  organisms/ml) and tested for sterility before use. These antigens were used without further treatment as unheated antigen or were boiled for 5 minutes and used as heated antigen.

The antigens for use in the absorptions were prepared from cells grown on tryptose phosphate agar in culture bottles. These were washed from the surface with saline, centrifuged and used with no further treatment in the case of the unheated antigen. The heated antigen was boiled for 5 minutes before the suspension was centrifuged.

The antigens used in the tube agglutination tests were prepared similarly to those used for the absorptions except that the suspensions were adjusted to the No. 3 McFarland nephelometer and stored in the refrigerator at 5 C until used.

**Antisera.** The antisera were obtained from 2.5 to 3.0 kg rabbits following serial intravenous inoculations. The rabbits were exsanguinated by intracardiac puncture after trial bleeding showed the antiserum to be of sufficiently high titer. The blood was collected in sterile bottles, allowed to coagulate at room temperature and stored at 5 C overnight. The serum was harvested by pipet, preserved with Merthiolate (brand of thimerosal) (1:10,000) and stored at 5 C.

**Absorption.** The absorptions were performed by slurring the desired amount of diluted serum (1:10) with the proper absorbing antigen in equal parts. The mixture was incubated at 45 C for two hours with periodic agitation. This suspension was centrifuged to remove the cells and the serum tested for activity against

the absorbing antigen by the slide agglutination test. This procedure was repeated until all unwanted antibody had been removed

**Agglutination tests** The slide agglutination test was performed according to the technic described by Ewing <sup>6</sup>

The tube agglutinations were accomplished by preparing two fold dilutions of the serum and adding an equal volume of the antigen. After thorough mixing the tubes were placed in a 37 C water bath overnight. Titers include the further two fold dilution by the antigen.

## RESULTS

The agglutination titers of the six sera were determined against heated and unheated homologous antigens and against the two related heterologous types as well as *Shigella dysenteriae* 1 and *Alkalescens Dispar* 01. These titers are presented in table 1. The unheated 891 antigen has an active heat labile blocking substance which severely inhibits the antigen antibody reaction in the homologous and heterologous sera. This phenomenon is hardly observed with strain 2499 and slightly so with strain 3162. The antigen related to *S. dysenteriae* 1 appears to be altered by heating as this agglutinin is reduced in quantity in sera against the heated 891 type antigens. This is a demonstration of a K antigen associated with the 891 type and *S. dysenteriae* 1. Such treatment on the other hand has little effect on the titers against A D 01 antigen.

TABLE 1. Serum agglutination titers of sera against 891, 2499 and 3162 antigens and *S. dysenteriae* 1 and *Alkalescens Dispar* 01.

Serum	Antigen									
	891 h	891 d	2499 h	2499 d	3162 h	3162 d	<i>S. dys.</i> h	<i>S. dys.</i> d	<i>Alk. 1</i> h	<i>Alk. 1</i> d
891 unh ed	40	5120	5120	5120	160	640	1280	2560	5120	5120
891 h ed		5120	5120	5120	160	5120	40	40	5120	5120
2499 unh d	160	5120	5120	5120	320	1280	160	320	40	2560
2499 h d		5120	5120	5120	80	320			2560	2560
3162 unh d	40	5120	5120	5120	2560	5120	320	1280	2560	2560
3162 h ed	40	5120	320	5120	5120	5120	80	80	2560	2560

Absorption with *S. dysenteriae* 1 or with A D 01 removes the inhibition of the agglutination with the unheated homologous and heterologous type organisms to varying extents (tables 2 and 3). Absorption with A D 01 demonstrates a relationship between these organisms by causing in most cases, a marked decrease in the

titer Absorption by a combination of these two antigens causes a greater lowering of titers

TABLE 2 Titration of b b d d b b d t  
p p d g t h t d t 891

T g	Ab b n g t g						
	U b b d	S dy t l	Alk l D p 01	2499 nh t d	2499 h t d	3162 h t d	3162 h d
891 h d		5120	1280		20	80	
891 h d	5120	5120	320		20		
2499 unh t d	5120	1280	640		80		
2499 h d	5120	5120	640				
3162 unh t d	160	40					
3162 h d	5120	2560	640				
S dy l	40						
Alk l D p 01	5120	5120					

TABLE 3 Titration of b b d d b b d t p p d p t  
b t d t 3162

T g	Ab b n g a n t g						
	U b b d	S dy t l	Alk l D p 01	891 unh t d	891 h d	2499 h d	2499 h t d
891 h d	40						
891 h d	5120	2560	640				
2499 unh d	320	5120	640				
2499 h d	5120	1280	640				
3162 unh	5120	5120	2560				
3162 h d	5120	5120	2560				
S dy l	80		160				
Alk l D p 01	2560	5120					80 20

Reciprocal absorptions of the 891 type sera removes the anti body more efficiently than absorption with *S. dysenteriae* 1, or A D 01 alone or absorption with both. However, strain 891 possesses a minor antigen not possessed by 2499. Nearly all *S. dysenteriae* 1 reacting sites and a large percentage of the A D 01 sites are removed by reciprocal absorptions with the type organisms. These reactions indicate there are some specific antigenic differences among the three related types.

Agglutination tests with antigens of the Flexner and Boyl groups were negative except for the nonspecific Flexner Y. There were minor cross reactions with A D 02 and A D 03.

In some further examinations it was found that strain 891 has antigens related to *Escherichia coli* strains 01 064, and 069. Strain 891 effectively removes agglutinins from antisera prepared against *Esch. coli* strains 01a and 064 (table 1). Absorptions were not carried out on coli 069 antiserum as the initial agglutination was of very low titer in 891 serum or when 891 was tested in this serum.<sup>7</sup>

TABLE 4 The effect of reciprocal absorption upon the titer of antisera prepared against strain 891 and *Escherichia coli* strains 01a and 064

Serum	Absorbing antigen	Test titer				
		Str 891	<i>S. dysenteriae</i> 1	Alkali cells D spar 01	<i>E. coli</i> (US-41)	<i>E. coli</i> 064
Str 891	Negative	20 480	640	20 480	20 480	2 560
	<i>E. coli</i> US-41	1 280				
	<i>E. coli</i> 064	10 240				
<i>E. coli</i> US-41 O1b	Negative Str 891	20 480	80	20 480	20 480 40	320
<i>E. coli</i> 064	Negative Str 891	20 480		1 280	1 280	20 480 20 480

Titer not determined between multiple agglutination by individual agglutinates



## DISCUSSION

It can be expected that in the examination of large numbers of isolates from an epidemic disease a small percentage of the cultures will be aberrant. The three organisms described here represent a group of 10 cultures received in this laboratory during the summer and fall of 1951.

The organisms described in this report do not comply with the description of any currently described member of the genus *Shigella* although based on preliminary cultural characteristics they appeared to be members of this genus. Upon further investigation it was found that the organisms possessed antigenic relationship with A D 01 and *S. dysenteriae* 1 although the biochemical reactions conformed to neither of the antigenic types. Subsequent serologic studies indicated the organisms to be more closely related to A D 01 in that major antigens were shared. On the other hand only minor antigenic relationships between the 891 type and *S. dysenteriae* 1 occurred. The antigenic relationship of the 891 type to *S. dysenteriae* 1 is the same as that of A D 01 to *S. dysenteriae* 1. As would be expected approximately the same degree of cross agglutination was encountered between the 891 type and *Esch. coli* 01 a b as with A D 01.

Ewing has pointed out the necessity for considering the serologic results of the various tests as more important than the biochemical while not allowing the systematics to become so cumbersome as to be impractical. There have however been numerous reports concerned with the antigenic heterogeneity of the genus *Shigella* and related groups. Mackie found *Esch. coli* to cross react with various members of the Flexner and Sonne groups. Stuart and associates described major antigenic interrelationships between *Esch. coli* and the A D 01 as well as between paracolon bacilli and A D 01. A minor relationship was observed between A D 01 and *S. flexneri* serotypes. Ewing, Hucks and Taylor reported a cross relation between the *Shigella* like organism (70) and *Esch. coli* 0112 a b. Ewing reported a wide range of interrelationships between the various serotypes of *Shigella* and the members of the Alkalescens Dispar group and the 0 group serotypes of *Esch. coli*.

Wheeler and Stuart in a study of the mannitol negative group of the genus *Shigella* found there was some degree of agglutination of A D 01 in *S. dysenteriae* 1 antiserum. The 14 strains of A D 01 tested were agglutinated to appreciable titers in 7 of the 8 *S. dysenteriae* 1 antisera and to a low titer (1:40-1:80) in the eighth antiserum.

The exact taxonomic position of this group of organisms is not clear. Ewing and Kauffmann have made the suggestion that no new serotype be added to the Alkalescens Dispar group of the genus *Escherichia* but that new serotypes be classed as

anaerogenic nonmotile coliform organisms. As there is an antigenic fraction which is not removed by absorption by A D 01, these strains probably can not be grouped among the A D 01 but should be placed with the anaerogenic nonmotile coliform organisms. This disposition would also take into account the differences in biochemical activity. However, in view of the close antigenic relationship to A D 01 it is proposed that this group of organisms be identified as *Alkalescens Dispar* 01 var *Kojii*, this designation being a provisional one.

### SUMMARY

A group of organisms, provisional serotype *Alkalescens Dispar* 01 var *Kojii*, related to *Shigella dysenteriae* 1 and A D 01 serologically but differing in biochemical reactions has been described. The taxonomic position of these organisms has been discussed in the light of the current views on the systematics of the genera, *Shigella*, *Escherichia*, and the *Alkalescens Dispar* group.

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# USE OF CAPILLARY TUBING FOR APPLYING ACID IN VERRUCA THERAPY

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**I**N the past 20 years the writer has run the gamut of techniques in the treatment of verruca plantaris—potential cautery with acids cryotherapy curettage under local anesthesia et cetera. In search of an efficient method of applying strong acid solutions to plantar warts the writer first pursued a technic at the U S Naval Training Center Bainbridge Md which further developed at this dispensary has produced excellent results. The method allows for complete control of the acid employed in regard to quantity used penetration into the tissues and application to the very marginal limits of the lesion.

I prefer to use trichloroacetic or bichloroacetic acid (saturated solutions) as the destructive agent. These two acids although strong enough to devitalize the tissues do not cause the violent reaction sometimes produced by monochloroacetic acid.

The superficial cornified layers of the verruca are first pared off with a scalpel as closely as possible but with the production of little or no bleeding. Then instead of applying the strong acid solution to the surface of the lesion with the customary pointed wood applicator a standard small glass coagulation capillary tube (75 mm long 1.0 mm inside diameter) is employed.

The trichloroacetic acid solution will rise inside the tiny tube by capillary action when the tip end of the tube is immersed in the bottle of acid. By observing the level of the liquid in the tube it is simple to determine how much of the acid is being used. I generally employ an acid column in the coagulation tube of about 3/4 inch in height. A large drop of the trichloroacetic acid solution may be noticed hanging at the very tip or flowing down along the side of the glass tube upon its withdrawal from the bottle. This should be wiped off with a quick stroke against a towel paper or gauze sponge.

When a pointed wood applicator is used to apply acid to the skin, some of the acid is absorbed by the wisp of cotton that may be wound about the applicator tip and also by the wood of the applicator itself. Some control in applying the acid to the tissues is thus lost. This absorption of acid cannot occur when using the glass capillary tube as the applicator.

Proceeding with the technic the tip end of the tube is brought to bear against the surface of the verruca. On contact with the tissue, a small amount of trichloroacetic acid will leave the tube and moisten the surface of the lesion. As in the well known manner of pricking the verruca with a pointed wood applicator, the capillary tube is repeatedly pressed against the tissue. As this procedure is pursued, the acid will continue to emerge slowly and will be seen to settle lower and lower in the tube until it is completely spent. If at any time it is desired to expel any or all of the acid from the tube, the tip end can be touched against a towel or gauze sponge. This maneuver will withdraw liquid from the tube in the manner of a blotter.

The repeated pricking of the lesion with the tip of the tiny glass tube will puncture the surface of the verruca and thus permit deeper penetration of the acid. Due to the rapid action of the trichloroacetic acid at the same time the disintegration of the tissue is readily observed during the application. Furthermore the use of the capillary tube technic permits application of the acid to the very margins of any verruca regardless of configuration.

In some cases a pause of a minute or so in the procedure is desirable to allow destructive action in the tissues to proceed. After this momentary wait, resumption of the pricking process for another minute or half a minute will produce greater amount of destruction of involved tissue.

Some slight pain that may be experienced during the application will generally cease immediately upon termination of the actual pricking of the tissues. At worst, when considerable acid is applied at one sitting to cause rapid destruction of the growth a stinging sensation may persist for an hour or so following treatment. This pain factor can be controlled by the operator, because he decides whether to apply only one or more than one capillary tube "dose" during the course of an application.

Following treatment the verruca is covered with a dry dressing usually an adhesive bandage and the patient is advised to keep the lesion dry for the first day or two. The second treatment—curetting the devitalized tissue and reapplying the acid—usually is given 8 to 10 days later. If necessary further treatment can be given after a similar time interval.

Generally, after a few treatments the patient will state that the verruca is no longer painful. The lesion will appear dehy-

drated and devitalized the overlying tissue may be dark in color. Usually the acid is not reapplied at this time and the patient should be scheduled for re-examination in two weeks. If after two weeks some wart tissue still remains the verruca should be touched up again as the occasion demands.

Only three or four applications of the trichloroacetic acid have been required to eradicate most of the verrucae treated. Some cases have been cleared after only two applications and some after only one. In two of approximately thirty cases treated five applications of the acid were necessary for complete eradication.

The method of application described has been used successfully in the treatment of both single and multiple verrucae. It has been employed not only in cases involving previously untreated verrucae but also in those cases that have recurred following previous treatment. It appears to be a valuable technic for the treatment of the small satellite type of wart which sometimes appears following surgical removal of a larger verruca. The method has not been attempted in those cases of verruca that have recurred following previous treatment by roentgen radiation.

During the procedure of pricking the verruca clogging of the tiny capillary tube caused by a backing up of some of the devitalized tissue may occur. In such event the tube should be discarded for another or the clogged portion may be broken off by holding the clogged part of the tube between the folds of a 4 by 4 inch gauze sponge. After fracture the fresh end of the tube should be wiped clean with a stroke of the sponge.

Capillary tubes generally are stocked in two lengths 75 mm and 150 mm packed 100 to a container. The cost is very nominal. Tubes 150 mm or longer may be broken to desired lengths. The tip end of a broken length of tube always should be wiped clean before use. Incidentally the sharp end of a broken length of capillary tubing will more easily puncture the surface of the verruca permitting better penetration of the acid. Under control of one skilled in the technic this is a desirable feature.

This technic may have value in other dermatologic procedures. Variations of the technic and other effects will become apparent during its use.

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# AN ALKALINE TELLURITE LAURYL SULFATE SALT PLATE FOR THE ISOLATION OF VIBRIO COMMA

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**M**ANY media have been described for the isolation of cholera vibrios. Some while highly efficient are difficult to prepare, especially under field conditions. Others like the plate of Aronson and plain alkaline agar do not require special ingredients or elaborate procedures. Their selectivity is based on their high pH value, usually 9.2 to 9.6. The Aronson medium contains sucrose and starch as fermentable substances and Andrade's indicator.<sup>1</sup> The brand of starch used in this plate greatly influences the development of the color of the colonies. In addition, many other intestinal organisms will also grow on plain alkaline agar and on the Aronson medium. The most troublesome are *Pseudomonas*, *Alcaligenes* and certain coliforms which, furthermore, may carry partial antigens of cholera vibrios. *Proteus* and other *Enterobacteriaceae* frequently spread on the surface of freshly prepared alkaline media. Thus our desire was to find proper inhibitory substances for these basically excellent plating media in order to facilitate the primary isolation of cholera vibrios on them by the less experienced. Moreover, a way was sought to utilize ingredients which are present in most small laboratories equipped with American media and chemicals.

The first inhibitory substance considered was potassium tellurite, used successfully by Gohar and Maklawi<sup>2</sup> in their enrichment fluid during the 1947 cholera outbreak in Egypt. To our knowledge it has not been tried as yet in solid media. It is readily available in the form of tellurite blood solution (Difco Laboratories or Baltimore Biological Laboratory) which is used for the preparation of diphtheria plates. This solution consists of defibrinated beef blood with 1 per cent potassium tellurite.

The second ingredient was sodium lauryl sulfate which is widely used in a broth for the detection of coliforms. Sodium lauryl sulfate was shown by Bavliss and Halvorson to have germicidal properties and to clear cultures including those of vibrios. In the present experiments it was used in a 0.1 per cent aqueous solution.

Venkatraman and Ramakrishnan advocated the use of sea salt in liquid media exceeding the concentration of sodium chloride employed in most medical bacteriologic media, i. e. 0.5 per cent. An increase of the salt concentration was therefore also included in this study.

Finally bile and bile salts are frequently incorporated into cholera media. In the experience of these writers vibrio colonies grown on such media are often larger than those grown on plain agar or on Aronson's culture medium. Ox bile (Arrow) was used in our comparative studies.

As the base for the media blood agar base (Difco or B. B. L.) was used. This is available in the majority of laboratories. It incorporates a sufficient amount of a peptone which greatly favors the growth of vibrios. It contains 1 per cent tryptose or thiotone, 0.5 per cent sodium chloride and beef heart infusion. Preliminary experiments showed that autoclaving of the base is not necessary if the inhibitory agents are added immediately and plates are poured without delay.

As test organisms two freshly isolated strains each of *Inaba* (O<sub>1</sub>av<sub>1</sub>) and *Fl. Tor* vibrios were used. *Aerobacter aerogenes*, *E. coli*, *Proteus morganii*, *Pseudomonas aeruginosa* and *Acillus subtilis* strains were selected to make up the test flora or the contaminating flora. The strains chosen for the experiment grew vigorously on plain agar. The *Proteus* and the *Aerobacter* used throughout this investigation had a tendency to spread over the surface of the plates to a certain extent. This was probably due to the changes in the pH of the media resulting from the utilization of some ingredients by these organisms.

The test strains were kept on agar slants and inoculated into separate broth tubes the day before use. After overnight incubation at 37°C the cultures were washed off with saline and standardized to contain 100,000 to 120,000 organisms per ml. For the simple growth test 0.1 ml of each suspension was dropped on the surface of separate plates and spread out using the clock streak. When plates with artificial stools were examined equal volumes of standardized suspensions of the contaminating flora were mixed with the respective *Vibrio* culture and the plates inoculated in the same manner as for the simple growth test.

The evaluation of the results was based on (1) inhibition of organisms other than vibrios, especially the blocking of spreaders, (2) colony size, and (3) serologic reactions of the *Vibrio* colonies

Colony size was determined by averaging the diameters in millimeters of 10 isolated colonies. Serologic testing was carried out by the plate method, using single factor sera prepared in this laboratory

In preliminary experiments, ox bile was excluded. It did not inhibit vibrios but stimulated the growth of *A. aerogenes*, *Proteus* and *Pseudomonas* to such an extent that they interfered with the easy isolation of vibrios. While bile and bile salts are known to enhance the multiplication of *Esch. coli*, this was not noticeable with the strains used in these experiments

Neither tellurite blood solution nor sodium lauryl sulfate could inhibit completely the growth of the contaminating flora in concentrations to 0.2 per cent tellurite blood solution and 0.01 per cent sodium lauryl sulfate separately or in combinations. These amounts were the maximums tolerated well by vibrios without a diminishing of the colony size. Using different concentrations of sodium chloride, sucrose as a carbohydrate source, and changing the pH, the results shown in table 1 were obtained

Table 1 shows that this combination plate is most selective when made up as follows with sodium chloride concentration of 1.5 per cent which is the average of the concentrations shown in the eighth and ninth columns under pH 9.6

Dissolve blood agar base (Difco or B. B. L.)	40 grams
in distilled water	800 ml
by heating in a boiling water bath. Add	
Sodium chloride	15 grams
Shake until dissolved then add	
10 per cent sodium carbonate	50 ml
Check pH. It should be 9.6. Then add	
20 per cent sucrose	50 ml
0.1 per cent sodium lauryl sulfate	100 ml
Let cool to about 75° C. then add	
Tellurite blood solution (Difco or B. B. L.)	2 ml

Keep at 75° C. for a few minutes then cool to about 50° C. and pour into petri dishes about 20 ml per dish

The plates should be used within three days. They have to be stored in a cool place



TABLE I

		b		c		d		e		f		g		h		i		j		k		l		m		n		o		p		q		r		s		t		u		v		w		x		y		z		aa		ab		ac		ad		ae		af		ag		ah		ai		aj		ak		al		am		an		ao		ap		aq		ar		as		at		au		av		aw		ax		ay		az		ba		bb		bc		bd		be		bf		bg		bh		bi		bj		bk		bl		bm		bn		bo		bp		bq		br		bs		bt		bu		bv		bw		bx		by		bz		ca		cb		cc		cd		ce		cf		cg		ch		ci		cj		ck		cl		cm		cn		co		cp		cq		cr		cs		ct		cu		cv		cw		cx		cy		cz		da		db		dc		dd		de		df		dg		dh		di		dj		dk		dl		dm		dn		do		dp		dq		dr		ds		dt		du		dv		dw		dx		dy		dz		ea		eb		ec		ed		ee		ef		eg		eh		ei		ej		ek		el		em		en		eo		ep		eq		er		es		et		eu		ev		ew		ex		ey		ez		fa		fb		fc		fd		fe		ff		fg		fh		fi		fj		fk		fl		fm		fn		fo		fp		fq		fr		fs		ft		fu		fv		fw		fx		fy		fz		ga		gb		gc		gd		ge		gf		gh		gi		gj		gk		gl		gm		gn		go		gp		gq		gr		gs		gt		gu		gv		gw		gx		gy		gz		ha		hb		hc		hd		he		hf		hg		hi		hj		hk		hl		hm		hn		ho		hp		hq		hr		hs		ht		hu		hv		hw		hx		hy		hz		ia		ib		ic		id		ie		if		ig		ih		ii		ij		ik		il		im		in		io		ip		iq		ir		is		it		iu		iv		iw		ix		iy		iz		ja		jb		jc		jd		je		jf		jg		jh		ji		jj		jk		jl		jm		jn		jo		jp		jq		jr		js		jt		ju		jv		jw		jx		jy		jz		ka		kb		kc		kd		ke		kf		kg		kh		ki		kj		kl		km		kn		ko		kp		kq		kr		ks		kt		ku		kv		kw		kx		ky		kz		la		lb		lc		ld		le		lf		lg		lh		li		lj		lk		ll		lm		ln		lo		lp		lq		lr		ls		lt		lu		lv		lw		lx		ly		lz		ma		mb		mc		md		me		mf		mg		mh		mi		mj		mk		ml		mm		mn		mo		mp		mq		mr		ms		mt		mu		mv		mw		mx		my		mz		na		nb		nc		nd		ne		nf		ng		nh		ni		nj		nk		nl		nm		nn		no		np		nq		nr		ns		nt		nu		nv		nw		nx		ny		nz		oa		ob		oc		od		oe		of		og		oh		oi		oj		ok		ol		om		on		oo		op		oq		or		os		ot		ou		ov		ow		ox		oy		oz		pa		pb		pc		pd		pe		pf		pg		ph		pi		pj		pk		pl		pm		pn		po		pp		pq		pr		ps		pt		pu		pv		pw		px		py		pz		qa		qb		qc		qd		qe		qf		qg		qh		qi		qj		qk		ql		qm		qn		qo		qp		qq		qr		qs		qt		qu		qv		qw		qx		qy		qz		ra		rb		rc		rd		re		rf		rg		rh		ri		rj		rk		rl		rm		rn		ro		rp		rq		rr		rs		rt		ru		rv		rw		rx		ry		rz		sa		sb		sc		sd		se		sf		sg		sh		si		sj		sk		sl		sm		sn		so		sp		sq		sr		ss		st		su		sv		sw		sx		sy		sz		ta		tb		tc		td		te		tf		tg		th		ti		tj		tk		tl		tm		tn		to		tp		tq		tr		ts		tt		tu		tv		tw		tx		ty		tz		ua		ub		uc		ud		ue		uf		ug		uh		ui		uj		uk		ul		um		un		uo		up		uq		ur		us		ut		uu		uv		uw		ux		uy		uz		va		vb		vc		vd		ve		vf		vg		vh		vi		vj		vk		vl		vm		vn		vo		vp		vq		vr		vs		vt		vu		vv		vw		vx		vy		vz		wa		wb		wc		wd		we		wf		wg		wh		wi		wj		wk		wl		wm		wn		wo		wp		wq		wr		ws		wt		wu		wv		ww		wx		wy		wz		xa		xb		xc		xd		xe		xf		xg		xh		xi		xj		xk		xl		xm		xn		xo		xp		xq		xr		xs		xt		xu		xv		xw		xx		xy		xz		ya		yb		yc		yd		ye		yf		yg		yh		yi		yj		yk		yl		ym		yn		yo		yp		yq		yr		ys		yt		yu		yv		yw		yx		yy		yz		za		zb		zc		zd		ze		zf		zg		zh		zi		zj		zk		zl		zm		zn		zo		zp		zq		zr		zs		zt		zu		zv		zw		zx		zy		zz	
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One hundred fifty *Vibrio* strains were tested on this medium. All of the 31 Inaba cultures, 44 of the 46 Ogawa strains, 25 of the 26 El Tor types, 4 of the 5 Hikojima organisms, and 9 of the 12 "nonagglutinable" vibrios grew well on the plate. The strains which failed to grow on the new medium were old stock cultures, while recent isolates multiplied vigorously.

Of the stock organisms which were not cultivable on the new plate, 1 Ogawa, 1 Hikojima, and 2 "nonagglutinable" vibrios, however, formed colonies on Aronson's plate.

When selected colonies grown on the new medium were typed with specific sera, the slide agglutination test gave rapid positive reactions in all cases.

All *Vibrio comma* showed translucent grayish colonies on the new medium in 20 to 24 hours, which turned blacker after longer incubation. Whitish gray colonies also were produced by *A. aerogenes* which, however, needed 40 to 48 hours to develop the gray discoloration. *Aerobacter* growth was always opaque, in contrast to the translucent *Vibrio* colonies. It is believed that this reduction of potassium tellurite is helpful in the recognition of vibrios. Experiments are being set up to check other intestinal organisms, especially *Enterobacteriaceae*, for their ability to give the same reaction.

Thirty stools received for routine examination from cases of diarrhea not involving vibrios were streaked to the new plate. They showed no growth of any organism in 24 hours.

Finally, the new plate was compared with Aronson's and with plain alkaline agar plating to it either vibrios alone or a mixture composed of an equal number of a *Vibrio*, an *Esch. coli*, an *A. aerogenes*, a *Pr. Morganii*, a *Ps. aeruginosa*, and a *B. subtilis* strain described in previous experiments. Measured amounts of this mixture to contain 3, 30, and 300 vibrios per inoculum (0.1 ml) were streaked to 10 plates each. The results are shown in table 2 as determined after 24 and 48 hours incubation.

The new plate proved itself very selective after 24 hours incubation. The contaminating flora did not grow in 24 hours. It became evident only after 48 hours while *Vibrio* colonies still could be selected from the surface of the media with ease. Vibrios formed smaller colonies on the new plate but the contaminating flora was suppressed to a great extent (table 2).

Admittedly, the plates were subjected to too severe tests by using a contaminating mixture composed of several non-fastidious organisms and checking against small numbers of vibrios. It is believed, however, that such testing will produce results which are less likely to crumble under the impact of field evaluation.

TABLE 2 C mp r i / l y / b t b m d

S d	I b d h ur	E p e d m b f g a n m l m									
		300		30		3		3 mm			
		N m b f b l b d / g d m t f l o n									
		A c n	Alk g	N w p l t	A c n	Alk g	N w p l t	A	Alk g a r	N w p l t	
I b	24	400/2 5	350/2 5	360/2	33/3	30/3 5	34/2	4/4	4/4	4/2	
O g w	24	300/2 5	320/3	290/1 5	29/3	29/3	31/2	3/3	3/3	3/2	
L i T	24	280/3	280/3	300/2	23/3	24/3 5	28/2	2 5/3	3 5/3 5	3/2	
V b p l											
g fl											
V b	24	S	S	330/1 5	S	S	35/2	S1/2	S	3/2	
	48	S	S n	330/2	S	S	35/2 5	S	S n	3/2 5	
C m	48	S	S	72/<0 5	S	S	3/<0 5	S	S	0/0	

Alk Alk l  
 Adj d 10  
 Adj d wh l mb  
 V b l d  
 S S gly p d g g wth

The new plate is not suggested as a sole medium for the isolation of vibrios. It appears to be feasible for use together with plain alkaline agar and, if possible, with Aronson's medium. It permits the growth of El Tor vibrios, in which aspect it differs from the excellent medium of Wilson and Reilly.<sup>7</sup> Although it is not believed to be superior to the Panja and Ghosh plate,<sup>8</sup> it is much easier to prepare. While most authorities agree that Panja's<sup>9</sup> method of filtration of the stools through a porcelain candle into a boric acid medium has not been surpassed by any other method of cholera culture,<sup>10</sup> the difficulties involved in filtering each specimen for several hours compel us to use plating media inoculated directly as well as from enrichment or preserving broths. Improvement and further development of the cholera plates are needed yet.

## SUMMARY

A medium consisting of commercial blood agar base with 0.01 per cent sodium lauryl sulfate, 0.1 per cent tellurite blood solution (equivalent to 1:100,000 potassium tellurite), a final sodium chloride concentration of 2 per cent, and 1 per cent sucrose at a pH 9.6 was described. This plate is feasible for the growth of *Vibrio comma* but inhibitory for other organisms commonly found in the intestinal tract. The grayish discoloration of the *Vibrio* colonies developing on this medium facilitate their recognition.

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### MODERN MEDICINE MAN ON TELEVISION

Along with many of the excellent reform in medicine that took place soon after the turn of the century was a definite attempt to educate manufacturers and the public regarding the dangers of advertising and selling medicines direct to the public. Not all editor or pharmaceutical manufacturer accepted these reforms but the influence of those who disregarded them was greatly lessened and they were ceaselessly looked upon with disfavor. Unfortunately those who continued direct dealing with the public soon began using the medium of radio for advertising and as the year went by radio became a recognized comping sedatives headache powders vitamins and numerous other medicines until the ears of the public rang with the constant din of its chatter. After radio came television which has brought the nearest medicine show to life. Just as the credulous grandfathers of the present generation found the Indian medicine man and old Doc Jones and his cure for rheumatism convincing so do their grandchildren find tired blood relieves headache twice as fast like a doctor's prescription and other ridiculous statements claim half truths and the associated entertainment concerning an incredible degree. Unfortunately the same factors are operating in the modern version as with the old Doc Jones show but where the previous generation held out two bits for a dollar for a bottle the grandchild frequently shell out five dollars and at infrequently come back for more and continue to do so for months.

—EDITORIAL

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# A SELF CLEANING DENTAL MIRROR

WALTER M. ORMES Jr Major DC USA

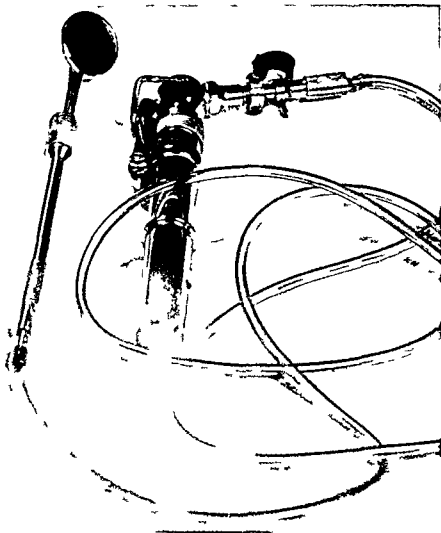
A distinguished oral surgeon stated during a series of lectures, "In any oral surgical procedure the operator must see well what he does to do well what he sees." This statement should never be forgotten, not only in oral surgery, but in all fields of dentistry.

With the advent of the water spray attachment for the dental handpiece, and then the high speed handpiece, the ordinary dental mirror became practically useless. An operator had the choice of working without the water spray and thus risking thermal damage to the pulp, or using the water spray and viewing the field of operation through a mirror showing a distorted image due to water and debris.

Operating without the water spray was the solution with a slow speed handpiece but with the high speed handpiece the cooling effect of the spray is a necessity to protect the pulp. It became apparent that the solution to the problem must lie in a mirror that would remain clear, while operating with the water spray attachment.

The idea occurred that if a stream of air could be made to strike the surface of a mirror the force of the air blast would blow away the water and debris and result in a clear image. Using a piece of plastic tubing 3 mm in diameter, a metal tip to fit the nozzle of the spray bottle air syringe and another metal tip to rest against the mirror and held in place with copper bands a fairly satisfactory air dried mirror was developed. This mirror although better than an ordinary mirror left much to be desired. The metal tip adjacent to the mirror being round, would not properly direct the flow of air the copper bands had a tendency to slip causing the tip and tubing to twist out of position and the instrument could not be sterilized without taking the bands off removing the plastic tubing and then reassembling after sterilizing.

Eventually the mirror illustrated in figure 1 was developed with the help of the Third Army Ordnance Section. The disassembled instrument is shown in figure 2. The easily removable mirror section is fabricated from cast aluminum with a flat tip



*F g 1 T b I f l a g d t l m r r o r a m b l d*

adjacent to the mirror proper so that the stream of air will sweep the entire surface of the mirror. The handle of the mirror is a hollow tube for passage of the air blast thus eliminating the copper band used in its prototype. The plastic tubing slips off the end of the mirror handle easily permitting sterilization of mirror and handle as a unit. The tube with tip for attachment to the air syringe shown in figure 2 and the clamp shown in figure 3 complete the instrument. This clamp is used to lock the air syringe in the on position.

This mirror has been used clinically with a high speed hand piece with built in water spray attachment and has been found to be satisfactory in both crown and bridge and operative pro-

cedures The air blast from the syringe keeps the surface of the mirror clean It requires only occasional wiping regardless of whether diamond stones, disks, or burs are used in the hand piece The noise of the air rushing over the surface of the mirror

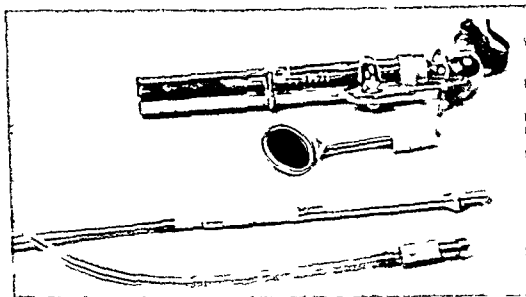


Figure 2 The instrument disassembled



Figure 3 Clamp used to lock a syringe in the "on" position

is not objectionable to the patient By tilting the mirror toward the tooth being operated on the field is dried for better observation in a matter of seconds The assistant by not having to operate the air syringe is freed for other duties

The mirror handle and tip can be made in any ordnance shop, and the plastic tubing and air syringe tip are available through Medical Supply The air syringe clamp can be made from a nail or piece of heavy wire



## SUMMARY

With the use of water spray handpiece attachments and high-speed dental handpieces the conventional dental mirror is practically useless. In order to obtain proper vision a mirror that is self cleaning must be used. The mirror described above is such an instrument. It is not difficult to manufacture is satisfactory in clinical use and has no maintenance or sterilizing problem.

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## WHY TELL THE PATIENT?

Standard textbooks of medicine supply excellent articles on recognized diseases but with rare exceptions the discussion fails to include one of paramount importance. No mention is made of the need for explaining to the patient the nature of his problem, the mechanism and significance of his symptoms and the course the illness may be expected to follow. This omission is unfortunate because with present day concentration on pathologic physiology in our medical schools the subject also receives little or no attention in clinical teaching. As a consequence it may be several years after graduation before a young internist appreciates all that can be accomplished by sufficiently detailed instruction of those under his care. There are two principal reasons why an explanation along the lines indicated is indispensable. In the first place it is an invaluable therapeutic tool of basic importance. Secondly it is one of the best available ways to show personal concern for the patient's welfare and therefore a most effective method for maintaining public support of our free enterprise system of medicine.

—A. CARLTON ERNSTENE, M.D.

*in Journal of the American Medical Association*  
p. 1110 November 2, 1957

# CHELATING SUBSTANCES IN MEDICINE

ROBERT B ABINGTON *Captain MC USA*

CHELATING substances have been used in industrial chemistry for many years, either as a means of inactivating a metallic ion or to assist in increasing the solubility of relatively insoluble metallic compounds. The term "chelation," however, was practically unknown to medicine until the end of World War II, when the medical implications of British antilewisite (BAL) were made known. The therapeutic uses of BAL have been limited to the treatment of poisoning or untoward reactions from certain heavy metals, namely, arsenicals, mercurials, and gold salts. Recent developments with newer chelating substances promise to be beneficial in the study and treatment of some of the more common maladies encountered in medicine.

The word "chelate" comes from the Greek word, *chēlē*, which means claw. This is extremely descriptive of chelating agents in that they possess the unique ability to combine with or "entrap" a metallic ion and inactivate it. In simple terms, the metallic ion reacts with the two ends of a short chained substance, thus creating a ring structure with the metallic ion tightly bound within the ring. In reality the structural mechanism is more complex, but the metallic ion always is bound within the molecular structure of the chelate from at least two sides. With the surrounding and binding down of the metallic ion, it is inactivated and isolated from further chemical reactions. This stable, readily soluble, metal complex then is easily removed from the body by normal renal function.

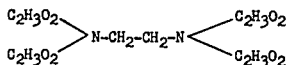
The theoretical implications of chelates and their effect on body metabolism are practically boundless. Any enzyme reaction utilizing a trace metal could be potentiated or inhibited by appropriate chelates depending on the degree of attraction for the specific metal that is necessary for the enzyme reaction.

Many of the drugs used in medicine are chelating agents. The list is too long to tabulate, but includes many of the antibiotics and the present-day antituberculosis drugs. The role that chelation plays in influencing the effectiveness of these drugs is poorly understood. A practical point concerning antibiotics is

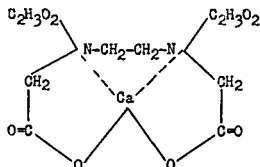
the chelation of aluminum and magnesium by the tetracyclines. The metal salt combination prevents absorption of the antibiotic from the gastrointestinal tract. The use of antacids containing aluminum or magnesium along with the tetracyclines therefore is considered unwise.

### EDTA

Ethylenediaminetetracetic acid (EDTA) the most potent chelating agent available today, was discovered in Germany by Pfeiffer and Schwartzbach. This relatively simple compound contains four acetic acid groups attached to ethylenediamine. The structural formula is as follows:



This substance has assumed clinical importance for many reasons. It is a potent chelator that is not metabolized and therefore may be used to remove calcium and certain toxic metals from the body. It is relatively nontoxic and inexpensive. In the presence of heavy metal or alkaline earth ions, EDTA reacts to form highly stable soluble metal chelate compounds. The structure of the calcium chelate may be depicted as follows:



As with other chelates, EDTA has a variable affinity for different metals depending on the dissociation or stability constant and the relative concentration of the exposed ions. In general, metals such as copper, nickel, and lead are bound more tightly than those of the alkaline-earth group, including calcium, magnesium, and barium. These alkaline earths in turn are bound to a much greater degree than the alkali metals, sodium, potassium, and lithium. Therefore, a sodium EDTA complex would be replaced in the body by a calcium complex. Likewise, a lead EDTA complex would be excreted unchanged in man.

For several years after its release on the American market, EDTA was believed to be a nontoxic drug with a wide margin of safety if used in the recommended dosage, but recent observations prompted a reappraisal of this drug and it now is established that EDTA may result in a toxic nephrosis. The hydropic degeneration of the proximal tubules is thought to be a reversible process if the drug is discontinued early enough.<sup>1</sup> Toxicity is related more to the duration of treatment than to the amount of drug used. The currently recommended dosage is 50 mg per kg for five days, followed by a rest period of at least two days. Daily urinalyses should be carried out if EDTA is used intravenously. The presence of acute or chronic renal disease probably should cause some reluctance in using this drug.

### CLINICAL INVESTIGATIONS WITH EDTA

**Lead Poisoning** Experimental trial of EDTA in patients with inorganic or organic lead poisoning has passed the investigational stage. It now has been accepted by most authorities to be the drug of choice. Calcium Disodium Versenate (brand of edathamil calcium disodium) is used to prevent the chelate from lowering the serum calcium. The alkaline metals (Na) and earths (Ca) are easily displaced by the heavy metal (Pb) within the body and excreted as the lead complex of EDTA.

**Hypercalcemia** Calcium is present in man in such large concentrations and has such a strong affinity for EDTA that hypocalcemia can be produced easily by injecting the chelate. EDTA therefore has been used in an effort to remove metastatic calcifications, calcium deposits around joints, calcified corneal opacities, calcified vascular plaques, renal calcifications, and other abnormal calcific deposits. Although reports are conflicting, it appears that calcium can be removed successfully<sup>2</sup> if this chelate is used properly over a prolonged period of time. It must be emphasized that the treatment results in only a transient benefit unless the underlying condition is corrected. Judicious use of EDTA seems particularly helpful in alleviating symptoms of hypercalcemic toxicity. Loss of symptoms and return of renal function were noted for several months in patients with hypercalcemia, advanced carcinomatosis, and renal failure.

**Coronary Atherosclerosis** The problems of existing coronary atherosclerosis and of how to increase needed blood supply to endangered tissues have been approached with EDTA. It is known that calcium is integrated with the cholesterol in an atheroma and thereby becomes an active participant in a living pathologic structure. By chelation of the calcium, it is believed that the organic atheromatous matrix might undergo disintegration. A recent study<sup>3</sup> of 20 patients with clinical evidence of advanced coronary atherosclerosis and progressive angina pectoris indicates that multiple infusions of EDTA may reverse the process.

in part. It appears that by repeated chelation of calcium within the body the symptoms and signs of vascular insufficiency caused by atheromatous plaques may be relieved for a significant period of time. Although cardiac stress tests were not used, serial electrocardiograms revealed reversion of the ischemic patterns to normal. This correlated with the clinical improvement of all patients. Of the 20 reported patients with angina pectoris, 19 survivors obtained unusual symptomatic relief that could not be attributed to any other source.

The only apparent hazard associated with this study was the possibility of a calcium embolus occurring. Rapid disintegration of an atheromatous plaque may cause fragmentation of the friable calcium cholesterol matrix and dislodgement into the blood stream. One reported autopsy seemed to confirm this.

The relationship and effect of chelating agents on atherosclerosis need considerable study and evaluation before any conclusions can be drawn.

**Treatment of Digitalis Toxicity.** Potassium *depletion* or calcium *excess* enhances the toxic effects of digitalis. Likewise calcium *depletion* or potassium *excess* have been found to prevent or abolish digitalis in induced cardiac arrhythmias. It is reported that injection of a small quantity of EDTA chelates some of the available calcium ions and quickly terminates arrhythmias resulting from digitalis intoxication. It is conceivable that EDTA or a similar chelate could replace potassium when a rapid intravenous medication is needed for cardiac arrhythmias secondary to digitalis toxicity.

**Radioactive Decontamination.** The majority of fission products of a nuclear explosion have a short half life and therefore pose no treatment problem, but those with a long half life present a chronic internal radiation hazard. Chelating substances have been employed to remove these radioactive metals from the body. EDTA and zirconium citrate are presently being tested by research laboratories. The effectiveness of this treatment depends to a great extent on the rapidity of administration of the chelate after exposure. Recent studies indicate that the most effective treatment for exposure to multiple fission products of a nuclear explosion consists of pretreatment with EDTA followed by zirconium citrate soon after exposure.

#### INVESTIGATIONS WITH OTHER CHELATES

**Radiation of Tumors With Chelates.** Uranium is said to be an excellent substance for the treatment of tumors. Neutron capture by  $U^{235}$  releases enormous amounts of energy over very short ranges in the form of fission particles. If fission were to take place in the tumor, the tumor might be completely destroyed.

In the past, clinical trials with this substance have not been possible because administration of this metal in the free state has resulted in serious kidney and liver damage.

Porphyrins are one of the many excellent chelates present in nature. It has been known that porphyrins concentrate heavily in tumors, and in embryonic and inflammatory tissues. Chelation of  $U^{235}$  with porphyrin would seem to be an ideal way to transport this substance to inaccessible tumors.  $U^{235}$  would then be activated by the neutrons from an atomic reactor. Early experimental studies indicate that the uranium porphyrin complex does not have the toxic properties of free  $U^{235}$ .<sup>6</sup> If this work is confirmed, it is possible that chelates will be invaluable in the treatment of cancer.

**Chelation of Ferrous Sulfate** By combining ferrous sulfate with a chelating agent, the almost universal intolerance to Fe has been overcome. Recently a new hematinic, an alpha aminoacetic ferrous sulfate complex, was studied.<sup>7</sup> By chelating iron within the molecular structure of the amino acid, it was found that the absorption of iron was increased markedly<sup>8</sup> and that gastric irritability from the ferric compounds formed in the stomach was prevented.

### SUMMARY

Chelating substances react with a metallic ion by encompassing the metal within the molecular structure and inactivating it. The affinity of a chelate for various metals depends on their stability constants and relative concentrations. Ethylenediaminetetraacetic acid (EDTA) is the most potent chelate presently employed, and its use is established as a good method for removal of certain heavy metals from the body. Recent clinical investigations of EDTA suggest possible benefit in using it in several different diseases, and the value of chelates as carriers of radioactive metals within the body is presently being studied.

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## CASE REPORTS

### Unilateral Renal Vein Thrombosis

ERNST R. MOELLER, Cpt MC USN

A CASE of unilateral renal vein thrombosis that was successfully treated is presented. While reviewing the literature it was noted that there were very few case reports in which therapy was instituted and in which the patient survived. In the vast majority of cases the condition was found at autopsy. It therefore was deemed pertinent to present this case not for the purpose of advocating new theories or treatment but rather to call the condition again to the attention of both pediatricians and urologists. Expedition in instituting therapy after the condition has been considered or verified is the prime factor in decreasing the mortality rate.

#### CASE REPORT

A Negro male infant, age 6 weeks, was seen in the outpatient department with the history of having had fever for the previous 18 hours and 2 generalized convulsions during this period. The previous evening at the onset of illness he had had a generalized convulsion and subsequently his mother noticed that he was feverish and listless. He slept fitfully during the night and in the morning had another generalized convulsion following which his mother brought him into the outpatient clinic.

The mother stated that during the past 48 hours she had noted some blood tinged urine and some pink staining of the diaper. No other symptoms were noted.

#### Past History

At birth the infant had been premature weighing 3 lb 13 oz, normal and in excellent condition. He had been hospitalized for one month and discharged weighing 5 lb. Physical examination at discharge revealed no abnormalities. Progress at home was normal until the onset of the present illness.

#### Family History

The mother and father were living and well and there was no history of disease. One sibling, age 3 years, had had convulsion with high fever.

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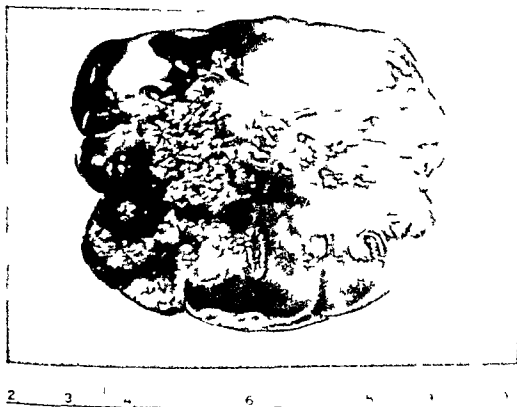


Figure 1 Gross appearance of infarcted right kidney



Figure 2 Cut surface of right kidney showing renal infarction. The infarcted area is the area between the two lines.



# Physical Examination

On admission to the hospital the infant weighed 5 lb 14 oz. He was mildly dehydrated and acutely ill. His temperature was 101.6 F. The physical examination was negative for unusual findings other than the abdomen which was moderately distended. In the right flank extending posteriorly there was an ill-defined mass about the size of a hen's egg extending from the costal margin downward and deep into the flank. There was also a mild paraphimosis.

# Laboratory Studies

The initial laboratory studies showed the following: red blood cell count 3,300,000 per  $\mu$ l, hemoglobin 8.5 grams per 100 ml, and white blood cell count 15,900 per  $\mu$ l with 38 per cent neutrophils and 62 per cent lymphocytes. Urinalysis revealed 4 plus albumin and microscopic examination showed 6 to 8 white blood cells, 4 to 5 finely granular casts, and numerous red blood cells. Radiographic examination of the chest, abdomen, and long bones was negative as were a spinal tap and a barium enema.

An intravenous pyelogram revealed an apparently normal left kidney and ureter. The picture of the right kidney was obscured but an area thought to be a single calyx was seen.

Preoperative support of the pyelogram instituted including a blood transfusion and on the following day exploration was performed. The left kidney and ureter were normal. The right kidney was enlarged, ecchymotic, and boggy. A right nephrectomy was performed.

# Pathological Findings

The specimen consisted of a kidney weighing 33 grams and measuring 5 by 2.5 by 2.5 cm. The capsule stripped with ease. The fetal lobulations were present and the surface was varicose. There were some areas of normal appearing kidney on the surface. Between these there were irregular dark red brown well demarcated zones (fig. 1). On cut section the parenchyma had small areas of normal appearing kidney interspersed between large zones of red-brown tissue. The line of demarcation between these areas was sharp (fig. 2). Several pyramids were dark red brown and were well demarcated from the overlying cortex.

Microscopic slides showed large areas of infarction throughout the kidney. Some of these involved only the medulla while others involved the cortex also (fig. 3). A thin zone of normal cortex remained next to the capsule in the area where infarction involved the cortex. Some of the infarcted areas showed necrosis with shadows of the former structures present while others were composed of fibrin areas of hemorrhagic extravasation with cellular necrosis. There was polymorphonuclear infiltration around the infarcts showing necrosis but no reaction was noted around the hemorrhagic portions. A thrombus showing evidence of organization was present in the renal vein. There also were multiple thrombi in the smaller veins in normal tissue.

### Postoperative Course

After a stormy postoperative 72 hours the infant tolerated fluids by mouth. The urine was clear on the 8th postoperative day. The blood urea nitrogen and creatinine were within normal limits when he was discharged from the hospital on the 16th day. Several follow up examinations revealed the infant to be progressing in a normal manner.

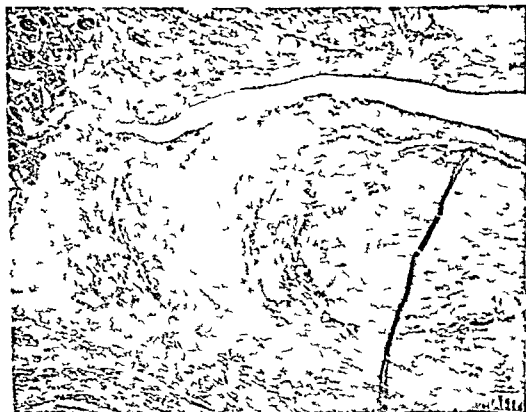


Fig. 3 Photomicrograph showing small and large thrombi ( $\times 48$ ) (Courtesy Armed Forces Institute of Pathology)

### DISCUSSION

The paucity of reported cases of renal vein thrombosis with recovery is evident in reviewing the literature. However, the importance of awareness of this condition is heightened by reports of survival after nephrectomy in at least 12 cases.<sup>1</sup>

The modern doctor usually is not so aware of the entity of acute thrombosis of the renal vein with renal infarction as was his predecessor of the nineteenth century who regarded thrombosis of the renal vein as a common occurrence in young infants.<sup>2</sup> It is not a common disorder in the pediatric age group, although it is not so rare as a casual survey might lead one to believe. Undoubtedly many cases pass unrecognized under the inadequate diagnosis of acute septicemia or acute pyelitis. At Babies Hospital (unit of Presbyterian Hospital) in New York City, 43 cases were found in 6,200 autopsies. 32 of these cases were in

the first year of life McClelland and Hughes encountered three cases of renal vein thrombosis with kidney infarction in 328 consecutive autopsies of infants under one year. In a recent review of the literature approximately 268 cases were recorded.

The syndrome may occur at any age but is uncommon beyond the age of 6 months. It has been found equally in both sexes.<sup>1</sup> Unilateral involvement occurred in 50 per cent of the cases and there was no apparent predilection to either side. The prognosis was grave in those cases in which both renal veins were thrombosed; however Fallon reported a recovery in one case. The mortality has been estimated at 95 per cent in unilateral cases without surgery and 90 per cent with surgery. Death usually occurs 48 to 72 hours after the appearance of the abdominal mass.

### ETIOLOGY AND PATHOGENESIS

An initial illness generally is conceded to be a predisposing factor in an overwhelming majority of the cases. In most instances diarrhea with associated dehydration, acidosis and collapse preceded or was concomitant with renal infarction. Barenberg and associates reported 5 cases occurring in a series of 25 infants who died in an epidemic of diarrhea of the newborn. Another group found 3 cases in 31 infants who died following severe diarrhea. Although ileocolitis is the principal predisposing factor, other infections that similarly alter the patient's electrolyte balance and hydration could cause renal thrombosis. Measles, scarlet fever, diphtheria, cutaneous infections and ophthalmitis were accused in several instances.

Many classifications of this pathologic entity have been advocated. The author believes that a more easily understood classification may be obtained by combining the ideas of Sandblom and Morison.

*Class I* Primary thrombosis of the renal veins that occurs in apparently healthy young infants.

*Class II* Secondary thrombosis of the renal veins that has been preceded by an acute illness, such as diarrhea. This is the most common variety.

*Class III* Thrombosis of the renal veins associated with renal inflammation.

The factors initiating the thrombosis are not known and at the present time we can only theorize as to the possibilities. Stasis of the blood stream undoubtedly is an important factor in intravascular thrombosis. It is well known that the renal tubules of the newborn have relatively little ability to remove water from the glomerular filtrate. This fluid lost by the glomeruli is not regained from the collecting tubules. At the same time the sick infant with vomiting and diarrhea rapidly becomes dehydrated with profound changes in the blood volume as well

as in the blood elements. This results in increased viscosity (hemoconcentration). The uniformly low arterial and capillary pressure and presumably low venous pressure in the neonate, in addition to the nature of the renal circulation with its double capillary network, results in considerable slowing of the stream. Therefore, the normal physiology of the young infant's glomerular system combined with the hemoconcentration, alteration of blood constituents, dehydration, and circulatory stagnation, may well favor intravascular clotting in the renal venules.

Apparently there is no defect in the clotting mechanism in these cases. No evidence has been presented that these infants are more susceptible to hemorrhagic phenomena than the normal newborn. Hepler<sup>10</sup> and Abeshouse<sup>7</sup> believed that the thrombus is formed by direct injury to the intima of the renal vessels; i. e., bacterial, mechanical, chemical, or toxic. These theories could explain the formation of the renal vein thrombosis in the sick infant, but it is difficult to apply them to the apparently healthy infant who suddenly becomes ill with this entity. Perhaps these infants have some intrinsic congenital anomaly of the renal system as the etiologic factor. This was suggested by Warren, Birdsong, and Kelley.<sup>11</sup>

#### PATHOLOGY

There is little agreement as to whether the smaller veins or the larger branches of the renal vein are first involved. Zuelzer<sup>12</sup> believed that in infancy the thrombosis is primary in the small radicles and may extend secondarily into the main branches of the renal vein or occur simultaneously in branches of small and large caliber. He found no evidence to indicate that retrograde extension of the thrombosis from the main stem of the renal vein played a part in the development of the process. Morison<sup>9</sup> expressed a similar viewpoint. Barenberg<sup>2</sup> reported two cases that had thrombi only in the main veins. The general consensus of opinion, however, is that both small and large veins are involved early and that the main vein is involved with the appearance of symptoms.

Infarction may or may not be present with a thrombosis, depending on the degree and rate of progress of the thrombosis. When massive infarction occurs the kidney is soft, boggy and deep purple or chocolate in color. Subcapsular hemorrhage with ecchymosis or hematoma usually is found. In localized thrombosis the segment involved is demarcated sharply by a zone of deep purple or chocolate color. Several observers<sup>3, 13</sup> found bacteria, notably streptococci, in the thrombus, but the majority have reported sterile cultures. The thrombotic or infarcted area, either segmental or total, usually involves the entire parenchyma with necrosis and loss of the renal architecture. Occasionally there is an extension of the thrombosis to the opposite kidney, down the vena cava to the iliac, pelvic, spermatic or ovarian veins, and upward to the pulmonary vascular tree and even the

cerebral sinuses<sup>3</sup> McClelland and Hughes reported that in their series the uninvolved kidney revealed lower nephron nephrosis

### SYMPTOMS AND SIGNS

The clinical manifestations of the disease as mentioned previously usually have been prefaced by or are concomitant with an acute infection. It is interesting to note that in the author's case no evidence of infection could be found. In most cases diarrhea associated with vomiting has been noted and has led to dehydration and peripheral collapse. Gross hematuria appears and the development of a tender somewhat tense mass is found in the flank. Occasionally gross hematuria is not present and because of the overwhelming sepsis or critical condition of the infant involvement of the urinary system may be masked or overlooked. Even in the absence of a palpable tender kidney the demonstration of albumin, pus and blood in the urine should arouse more than a passing suspicion.<sup>3</sup> Anuria or oliguria, acidosis and uremia are present in varying degree. Death usually occurs in a few days.

Excretory or retrograde urography will verify the diagnosis. Campbell and Matthews advised doing both procedures. The characteristic findings in excretory urography are a blotting out or absence of visualization of dye on the affected side when compared with the normal outline on the unaffected side. However, visualization of the urinary tract by intravenous pyelography in the newborn infant is notable for its inadequacies and may be valueless. Retrograde pyelography, although it was not done in this case, is probably the most useful procedure for diagnostic purposes. It will reveal isolateral bleeding or diminished function on the affected side. The ureterogram is normal with an associated compression or blotting out of the pelvic markings. With an increased amount of material injected into the ureter of the affected side, Campbell described an irregular diffusion of the media throughout the thrombosed organ as though the injection had been made into a mass of mush with no true pelvis outline demonstrated.

### DIFFERENTIAL DIAGNOSIS

The differential diagnosis should include adenomyosarcoma, polycystic kidney, hydronephrosis, acute pyelonephritis, renal or perinephritic abscess and renal dysplasia with cystic mass. Retrograde pyelography should establish the diagnosis.

### TREATMENT

Correction of shock, hydration, attention to electrolyte balance and blood transfusion, if necessary, are of utmost importance in preparing the patient for surgery. Immediately upon verification of the diagnosis following urography studies, the patient should be considered to be in an emergency status and preoperative preparation followed immediately by surgical inter-

vention, should be accomplished as quickly as possible. Nephrectomy of the thrombosed or infarcted kidney is performed. Abeshouse<sup>5</sup> emphasized that the surgeon should be certain to include the intravenous clot when the renal vein is ligated, to prevent extension of the thrombosis to the contralateral kidney. Rough and unnecessary handling of the renal pedicle should be avoided.

Postoperatively the judicious use of whole blood, fluids, electrolytes, and antibiotics as well as maintenance of an adequate caloric and protein intake, enhances the likelihood of successful management.

If both kidneys are involved, one can only offer supportive measures for a seemingly hopeless cause. Only one case of apparent bilateral renal vein thrombosis that survived has been reported.<sup>6</sup> One might consider employing anticoagulant therapy in such cases in an effort to hinder advancement of parenchymal damage as well as to discourage development of thrombotic phenomena elsewhere. If surgery is contemplated, however, the use of anticoagulant measures prior to surgical intervention should be discouraged.

#### SUMMARY

A case of unilateral renal vein thrombosis that recovered following nephrectomy is presented. Renal vein thrombosis should be suspected in all infants presenting the clinical picture of infection, dehydration, hematuria, and palpable tender mass in the flank. Prompt retrograde or excretory urographic studies are imperative. Immediate nephrectomy is mandatory following preoperative correction of the dehydration and electrolyte imbalance. The correct preoperative diagnosis of unilateral renal vein thrombosis is of less importance than the expeditious initiation of the above mentioned procedures.

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### DIAGNOSIS OF EXPEDIENCY

The appendix at birth h s a wide lumen and as the best insurance against obstruction nd dev lopment of acute inflammati this feature expl ins why acute app ndicitis is so rare n the neonate Within two years how ver th submucosal lymphoid tissue has developed to a great d gree reducing luminal d ameter and c eating a cause for the sudden increase in the incidence f cute appendicitis Th oppor tunity for ubclin al inflammation nd fibr sis beg us im mediatly That b th actual infect on of the appendiceal wall and s condary inflammatory response w thin the lymphoid t ssue to circulat g noxiou substances are common can be readily agreed upo th t the result ng intramural fibrosis cannot l ter be used as an expl nat on for clinic l illness h s been more difficult to accept The pressures the clinician feels in this rega d have to do with his natural compulsion to end up w th n o g nic d i gnosis f that is at all pos ible Chronic appendicitis like gastritis prol pse of the gastric mu osa a d many others b comes a diagn is of enforced expediency

—EDDY D PALMER M D

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# Heat Stroke A Review of Three Cases

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ROBERT L MASSONNEAU Ltutenant Colonel MC USA

**H**EAT STROKE is a state of hyperpyrexia associated with cessation of the body sweating mechanism. Prolonged excessive environmental heat is the principal etiologic factor. Humidity, wind velocity, acclimatization, and general physical condition, are other important contributory factors.<sup>1</sup> This condition is one of the few true medical emergencies for which treatment must be immediate to prevent death. The following patients were treated at this hospital during the summer of 1957, and have recovered from the effects of their sunstroke. We believe them to be of special interest because of the duration of their coma and the apparent dramatic efficacy of the treatment administered.

## CASE REPORTS

**Case 1** A 24 year old white man, a basic trainee with 22 days military service, was admitted to this hospital on 6 July 1957 at 1400 hours because of sudden loss of consciousness that had occurred one half hour previously. He had been on the rifle range from 0600 to 1200 hours that day at which time the environmental temperature was in excess of 100 F. He marched back to his company area and collapsed shortly after. Cold sponges were applied and he was evacuated to the hospital emergency ward.

*Physical examination* The patient was a comatose, well developed, obese white man in acute distress. His respirations were Cheyne-Stokes in type; his temperature was 107.8°F (rectally); pulse rate 180; blood pressure 120/80 mm Hg. The remainder of the physical examination was within normal limits except for absence of sweating and hot, dry skin.

*Laboratory studies* Admission laboratory data revealed a white blood cell count of 17,000 per  $\mu$ l with 80 per cent neutrophils. Hemoglobin was normal. Urinalysis revealed 1 plus glycosuria and albuminuria. The electrocardiogram was normal. Subsequent checks of these findings revealed no abnormalities. Results of electrolyte studies were normal. The serologic test for syphilis was negative and roentgenogram of the chest, taken later, was normal.

*Course in hospital* On arrival at the emergency ward the patient was immediately immersed in a bathtub of water containing ice chips.



and his temperature rapidly reduced. He was removed from the ice bath when his temperature was down to 100 F and was given 100 mg of hydrocortisone intravenously in dextrose and physiologic saline solution during the hours after admission followed by 100 mg of cortisone acetate intramuscularly every eight hours. At the time of removal from the ice bath his blood pressure was unobtainable and it was necessary to institute antihock therapy. He was given a solution containing Levophed (brand of l-norepinephrine) intravenously at a rate appropriate to maintain his blood pressure within normal limits. The foot of his bed was elevated and oxygen was administered by nasal catheter. It was necessary to support him by this means for the next 12 hours by which time the blood pressure had stabilized and Levophed was discontinued. Thorazine Hydrochloride (brand of chlorpromazine hydrochloride) 50 mg intramuscularly every four hours for two days was given with apparent effectiveness in reducing the extreme rigidity and struggling behavior which the patient exhibited. He remained comatose and unresponsive however and then displayed what appeared to be a typical picture of decerebrate rigidity. He required frequent nasopharyngeal suction to prevent obstruction but tracheotomy was not believed to be necessary. Approximately 30 hours after admission he began to respond to strong stimuli and occasionally muttered unintelligible responses. By the morning of 8 July after seeming to ascend through a gamut of basic neurologic states he was able to converse rationally and had good recall of events. On 9 July it was noted that his serum bilirubin at that time was 23.7 mg per 100 ml with 9.1 direct reacting and 14.6 mg per 100 ml indirect reacting. Thymol turbidity was 4.4 units. Cephalin cholesterol flocculation was one plus and serum cholesterol 164 mg per 100 ml with an esterified fraction of 80 per cent. Prothrombin time was 100 per cent and the SGO T was 325 units. Plasma hemoglobin and red cell fragility studies were normal. The liver was palpated 2 finger breadth below the costal margin and was lightly tender. On 15 July thymol turbidity was 6.2 units and 2-hour urinary urobilinogen was 1.2 units. The other tests were normal except for serum bilirubin of 14.2 mg per 100 ml with 8.5 indirect and 5.7 direct.

During the next month of hospitalization the jaundice gradually disappeared so that the patient had no residuals of his hepatitis. During the month however he showed various neurologic signs and symptoms. At times he had a positive Romberg sign and at times abnormal flex. He also showed extrapyramidal signs with tremor of the hands and head and pasticity of the extremities. He walked unsteadily for a few days after regaining consciousness but all these findings gradually improved.

The patient was given 30-day convalescent leave from 20 August to 19 September. On return he complained regularly of headaches and dizziness, pain in the right foot with difficulty in walking and other

symptoms which were very difficult to evaluate because of lack of supporting physical findings. Orthopedic and psychiatric consultations failed to disclose any other significant evidence of organic residuals. It was generally agreed that the patient had a passive aggressive personality pattern and was poorly motivated for further military service. Because a long-term medical and psychiatric evaluation seemed necessary he was transferred to an Army General Hospital and eventually was separated.

**Case 2** A 24 year old white man, a basic trainee on active duty 32 days, was admitted to this hospital on 6 July 1957 at 1930 hours in a comatose state. The patient had been on the firing range from 0800 to 1600 hours the day of admission, then marched back to his company area. At 1930 hours he suddenly collapsed and was brought to the emergency room. His skin was hot and dry and he was in shock. At the time of admission rectal temperature was 108 F, pulse rate 180, respirations rapid and blood pressure unobtainable. Physical examination was not otherwise remarkable.

**Laboratory studies** Admission laboratory tests showed urinalysis, serum electrolytes and chest roentgenogram to be within normal limits. An electrocardiogram was normal.

**Course in hospital** The patient was immediately placed in a tub of ice water. He became combative and disoriented. By 2000 hours his temperature had fallen to 101°F and the patient was removed from the ice bath and placed in bed. At 2005 hours his temperature was 97 F. He was extremely spastic and unresponsive and assumed a fetal position from which he could not be moved.

No further temperature elevation occurred during the remainder of the hospital course. The patient was given 50 mg of Thorazine intramuscularly and his spasticity decreased considerably. Intravenous administration of a solution of 5 per cent dextrose in saline containing 100 mg of hydrocortisone was instituted. He was given 100 mg of cortisone acetate intramuscularly every six hours for the next five days. He remained completely unresponsive and at approximately 2245 hours his blood pressure, which had returned to a level of 100/70 mm Hg, suddenly fell markedly and it was necessary to give Levophed intravenously at a rate appropriate to control shock. By 2345 hours the patient had become flaccid and areflexic. His blood pressure was controlled at levels of approximately 100/70 mm Hg by slow Levophed drip.

About five hours after admission the patient suddenly became responsive, sat up and asked for the doctor. He answered questions rationally and his neurologic examination at this time was normal. By the morning of 7 July 1957 it was possible to discontinue intravenous medication and he was able to take fluids by mouth. He progressively improved, was completely co-operative but had some persistent generalized weakness for several days. He was allowed to be ambulatory and went on a week end pass on 12 July 1957. His recovery was complete without residuals of physical or neurologic

and his temperature rapidly reduced. He was removed from the ice bath when his temperature was down to 100 F and was given 100 mg of hydrocortisone intravenously in dextrose and physiologic saline solution during the hours after admission followed by 100 mg of cortisone acetate intramuscularly every eight hours. At the time of removal from the ice bath his blood pressure was unobtainable and it was necessary to institute antishock therapy. He was given a solution containing Levophed (brand of norepinephrine) intravenously at a rate appropriate to maintain his blood pressure within normal limits. The foot of his bed was elevated and oxygen was administered by nasal catheter. It was necessary to support him by this means for the next 12 hours by which time the blood pressure had stabilized and Levophed was discontinued. Thorazine Hydrochloride (brand of chlorpromazine hydrochloride) 50 mg intramuscularly every four hours for two doses was given with apparent effectiveness in reducing the extreme rigidity and struggling behavior which the patient exhibited. He remained comatose and unresponsive however and then displayed what appeared to be a typical picture of decerebrate rigidity. He required frequent nasopharyngeal suction to prevent obstruction but tracheotomy was not believed to be necessary. Approximately 30 hours after admission he began to respond to strong stimuli and occasionally muttered unintelligible responses. By the morning of 8 July after seeming to ascend through a gamut of basic neurologic states he was able to converse rationally and had good recall of events. On 9 July it was noted that his sclera were icteric. Serum bilirubin at that time was 23.7 mg per 100 ml with 9.1 direct reacting and 14.6 mg per 100 ml indirect reacting. Thymol turbidity was 4.4 units. Cephlin cholesterol flocculation was one plus and serum cholesterol 164 mg per 100 ml with a nonturified fraction of 80 per cent. Prothrombin time was 100 per cent and the SGO T was 325 units. Plasma hemoglobin and red cell fragility studies were normal. The liver was palpated 2 fingers breadth below the costal margin and was slightly tender. On 15 July thymol turbidity was 6.2 units and 2-hour urinary urobilinogen was 1.2 units. The other tests were normal except for serum bilirubin of 14.2 mg per 100 ml with 8.5 indirect and 5.7 direct.

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## DISCUSSION

The foregoing cases of severe sunstroke are presented to illustrate the effectiveness of treatment in this condition. These patients were comatose for 30, 5, and 9 hours, respectively, and yet have apparently recovered completely from the effects of their sunstroke. All authorities emphasize that proper management of a case of sunstroke demands return of the patient's temperature to normal as rapidly as possible. This can be accomplished by immersion of the entire body in a tub of ice water until the temperature is almost normal (The tub and ice are kept ready for immediate use during the summer months.) Following the relief of hyperpyrexia, the patient must be adequately supported with proper nursing care, intravenous fluids in appropriate amounts, and control of blood pressure. Care must be taken that intravenous fluids not be administered too rapidly, for large quantities of fluid intravenously may precipitate pulmonary edema in these patients. For the management of hypotension during the critical phase, Levophed seems to be excellent. These patients also require frequent use of suction to avoid tracheal obstruction while in coma. Oxygen by nasal catheter serves to prevent hypoxia and to minimize the damage to the central nervous system that is caused by the hyperpyrexia and hypotension.

The condition of these patients was so serious that we used adrenocortical steroids, postulating that such severe trauma to the body must be associated with great adrenocortical stress and probably a significant degree of cortical failure or inadequacy. (This concept is neither proved nor controverted by pathologic findings. Malamud, Haymaker and Custer<sup>2</sup> reported the gross and microscopic changes in the brain, liver, adrenals, kidneys and other organs in a series of 125 autopsied cases. Hyperthermia *per se* was considered to be the proximate cause of the central nervous system damage, but findings in the parenchymal organs were of nonspecific etiology, were rare in cases of short survival, and could well have been secondary to hypoxia.) Thus, the use of exogenous steroids is based on the hypothesis of acute severe, functional adrenal depletion due to stress. We gained the distinct impression that the adrenal steroids were beneficial and possibly lifesaving in these patients. Sampson and Yuen<sup>3</sup> and Waugh<sup>4</sup> have previously described the use of steroids in such patients.

Jaundice, such as that noted in case 1, has been described previously<sup>5-7</sup> and attributed to hepatocellular damage, presumably due to hypoxia, possibly also to hyperthermia.<sup>8</sup> The clinical and laboratory findings did not support such considerations as acute hemolysis and Thorazine hypersensitivity as causes of the jaundice.

Electrocardiographic and electroencephalographic abnormalities have been reported. These examinations gave normal findings in case 1 and the electrocardiogram was normal in case 2.

The exact mechanism of heat stroke is unknown. However, there is considerable information which indicates that the problem results from fatigue of the heat regulation center.<sup>1,2,11</sup> It has been shown that prolonged exposure to heat with continuous perspiration gradually decreases the efficiency of the heat regulation center and the sweating mechanism of the body. If a person is able to obtain freedom from such an environment at intervals during the day, such as in an air conditioned room, heat stroke is not likely to occur. In the summer at Fort Hood, Tex., the temperature occasionally rises as high as 105 F and frequently does not drop below 80 F at night. The average humidity during the month of July 1957 was 79 per cent. The barracks were not air conditioned and hence the patients perspired 24 hours daily. Although heat precautions normally are taken and the commanders and noncommissioned officers are instructed in the cause and nature of heat injuries, all troops have not been adequately protected at all times.

The patients described were placed on the critically ill list and a fatal outcome was anticipated. Early and adequate treatment, including a vasopressor agent and adrenal steroids intravenously, apparently enabled them to recover completely. We report their cases to encourage vigorous therapy and a more optimistic prognosis in patients admitted for this condition in the future.

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# Fetus Papyraceous and a Microcephalic Infant

SAMP PATTERSON *Captain MC USA*

**F**ETUS PAPYRACEOUS is a rather rare condition in which one of twin fetuses has died and been pressed flat against the uterine wall by the living twin. Since Kindred<sup>1</sup> reviewed the literature in 1944 and summarized 150 cases, a number of additional cases have been reported.<sup>2-11</sup> The present case was not complicated by polyhydramnios as many are and nothing could be determined regarding the umbilical cord of the fetus or its relation to the placenta. In most cases, the compressed fetus is in the fundus, but here it was in the lower part of the uterus and delivered first. As in many other cases, the viable infant was abnormal.

## CASE REPORT

A 20 year old Caucasian woman was first seen in the prenatal clinic of this hospital on 27 February 1957. Her last normal menstrual period had been 12 October 1956 and her estimated date of confinement was 19 July 1957. She was para 2 gravida 3.

Past history on her initial visit revealed that she had had a kidney infection with one of her previous pregnancies and had had swelling of the feet and ankles with both pregnancies. Her first pregnancy terminated with delivery of a normal male infant 17 November 1954. She delivered a normal female infant 26 June 1956. There was no known viral infection during her present pregnancy.

On her initial clinic visit in February she weighed 136½ lb (usual weight 120). She was five feet tall. Her blood was type AB Rh positive with a hemoglobin of 12.4 grams per 100 ml. Her urine was negative for albumin and sugar on that visit and on each subsequent visit. The serologic test for syphilis was negative. On 18 June her hemoglobin was 12 grams per 100 ml. Her prenatal course was complicated by an excessive weight gain of 28 ¾ lb. At approximately seven months gestation the patient developed pitting edema of the feet and ankles. She was placed on a 1200-calorie low salt high protein diet and was given Diamox (brand of acetazolamide). The edema subsided for a few weeks but then recurred and persisted until delivery. During this period the patient's blood pressure remained normal and her urine negative for albumin. At no time during the prenatal

course was it thought th t she had twins o th t she had any evidence of polyhydramnios

She was dmitted t the labor suit 24 July in active labor with the vertex present ng her bl d pres ure was 116/80 mm Hg and the fetal heart t nes were normal n the left lower quadrant Labor prog ress d r pidly and she was taken to the delivery room two h ur aft r admision Rectal examin tion at that time reve l d the cervix to b d lated to a rim As the fetal head cam down quickly from a zero stati n to the p rineum a macerated fetus papyrac ous w s



Fig 1 M t d f tus papyr

suddenly xpell d f om the vag na It h d evidently been wedged betw n the viable infant s he d and the walls of the pelv s dur ng descent The viable twin was then d li e d from th r ght occipit anterio position ov a mdl n episiotomy Th fetu papyr ceou was bout 15 cm in length and 15 cm thick (fig 1) It w s very m erated bur well pre erv d The x w s not d temined The cond fetus we ghed 8 pounds 6 unces and w s a male (fig 2) Thi inf nt w s m cr ceph l c The pl cent w large but no weight w s ob tained It appeared normal with no ar s of nfar t on Alongsid one portion of the memb a c w a d i t rted a with ever l adhere t fragments of wh t m y h ve been th memb nes of th fetu p py

raceous. It could not be determined where the umbilical cord of this fetus might have entered the placenta.



Fig. 2. Fetus papyraceous with large microcephalic twin. This photograph unfortunately does not demonstrate the microcephaly.

The mother's postpartum course was uneventful. The infant took its formula well and was discharged with the parents, who were warned of the ultimate prognosis.

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### NO BED OF ROSES

Obstetrics is thought by many to be the most tagnant field in medicine. It is felt that nothing new ever happens and that it is a real bed of roses. The statement are far from my truth. We are constantly striving for and achieving a lower fetal and maternal mortality. We are improving our antenatal care. We are conducting our labors and delivery with better and safer analgesics and anesthetics. We are having more normal puerperium. Finally we are getting healthier mothers and babies. If one does obstetrics long enough he will find that the bed of roses padded with many obstetrical emergencies such as sudden severe hemorrhagic shocks of every description, disease of the parturient mother of every kind and difficult deliveries due to abnormal presentation.

—ROBERT W. ROSS, M.D.

*J. m l f th A k M d l S ty*  
p 196 Oct 1957

# Tracheoesophageal Fistula Without Atresia of Esophagus

## Diagnosis and Repair in the Newborn

PHILIP L. NOVA *Captain, MC USN*

**C**ONGENITAL tracheoesophageal fistula without other anomalies of the esophagus is relatively rare. In a combined series of 201 cases of congenital tracheoesophageal anomalies recently reported by Haight,<sup>1,2</sup> tracheoesophageal fistula alone was found in 3 per cent. In 1954 Ware and Cross<sup>3</sup> found 26 cases of this anomaly in the English literature, and added another one.

In newborn infants, the symptoms of tracheoesophageal fistula without other associated anomalies of the esophagus may not be too severe, and consequently may remain unsuspected. The life expectancy of most untreated cases is relatively brief, averaging from a few days to a few weeks, depending on the severity of the pneumonitis that develops.

The diagnosis, even when suspected, has presented some difficulties, but if certain measures are carried out during the roentgenologic examination with contrast medium, the diagnosis may be readily established. Once the diagnosis is made, surgical correction should be carried out as soon as possible.

### CASE REPORT

**Case 1** A white male infant, the second child of a 21 year-old mother, was born at this hospital on 18 August 1956. The prenatal course and delivery had been uncomplicated. His weight at birth was 8 3/4 lb, his cry was lusty, no resuscitative measures were used, and his general appearance was good. There was a considerable amount of mucus in the mouth, nose, and upper respiratory passages, and loud coarse rales were heard throughout both lung fields. There was no cyanosis.

During the first 24 hours of life the baby continued to have increased mucous secretions in the pharynx, although no fluids were given. On the second day he received a small amount of glucose solution by mouth. This promptly produced an episode of coughing, choking, and cyanosis. A small polyethylene tube was readily passed into the

stomach confirming patency of the esophagus and was left in the stomach for administration of glucose solution.

The preliminary roentgenographic examination revealed clear lung fields, no gross cardiac abnormalities, and an increased amount of air in the intestines (fig. 1). A small quantity of iodized oil was placed in the baby's mouth and roentgenograms taken in the conventional

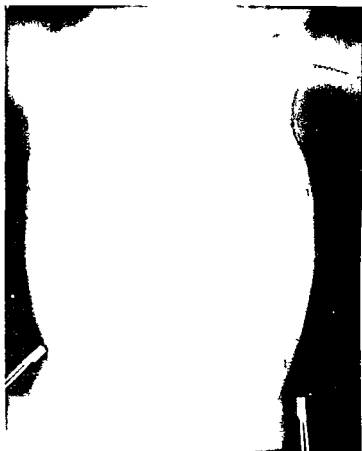


Fig. 1. Roentgenogram taken at 24 hours after birth. The baby had no gross abnormalities, and an increased amount of air in the intestines.

manner outlined the esophagus and stomach as well as the trachea and bronchi (fig. 2). No communication was demonstrated between the esophagus and trachea.

After the infant was returned to the nursery, several additional attempts were made to give him glucose solution by mouth. Each time this caused coughing, choking, and cyanosis. Because tracheoesophageal fistula was suspected, formula feeding was not given. The baby was kept hydrated by giving the glucose solution in small quantities through

the tube placed in his stomach. He tolerated this without difficulty, particularly when he was held in the upright position.

Additional roentgenographic studies were carried out on the third day. A small rubber catheter was placed in the stomach, and the baby held in the prone position on the x-ray table. Under fluoroscopic guid-



*Figure 2* Roentgenogram taken in the conventional manner with the baby in the supine position after a small amount of iodized oil had been placed in his mouth. The esophagus, trachea, and bronchi are well outlined, but the fistula was not visualized.

ance a small quantity of Lipiodol (brand of iodized poppy seed oil) was injected into the catheter as it was slowly withdrawn along the course of the esophagus. When the tip of the catheter reached the approximate level of the bifurcation of the trachea the contrast medium was seen to flow into the dependent trachea. Spot films taken at that point revealed a communication between the esophagus and trachea about 2 cm above the carina. The fistula was diagonally placed with the tracheal opening slightly above the opening in the esophagus (fig. 3).

Operation and repair of the fistula was performed on the following day. A right transpleural approach was used under endotracheal anesthesia. The tracheoesophageal fistula was found on the right lateral wall of the trachea 2 cm above the bifurcation; it was about  $\frac{1}{2}$  cm in length and 2 to 3 mm in diameter. Its tracheal connection was elliptic in shape. To facilitate closure it was transected with a wider



Fig. 3. Right transpleural approach with the baby held in the prone position. The dilated wall of the trachea is clearly demonstrated.

cuff on the tracheal side. The opening in the trachea was closed with a single row of interrupted sutures of No. 00000 atraumatic silk and the suture line was covered with a small flap of mediastinal pleura. The opening in the esophagus was closed in two layers using interrupted sutures of No. 00000 atraumatic silk.

The baby's subsequent immediate postoperative course and convalescence were uncomplicated. A diluted formula feeding was given orally beginning on the third postoperative day. He was discharged

from the hospital on the 15th postoperative day all feedings being taken without symptoms

He was seen at periodic intervals in the outpatient clinic and his growth and development continued normally. At 6 months of age his weight had increased to 14 lb 10 oz and he continued to be free of symptoms.

### DISCUSSION

The majority of congenital esophageal malformations consist of an atresia that usually is associated with a fistulous communication between the trachea and lower esophageal segment. The various types which occur have been well documented. According to Vogt's<sup>4</sup> classification, these are

Type I—Complete absence of the esophagus

Type II—Atresia of the esophagus with an upper and a lower esophageal segment, each ending in a blind pouch

Type III—Atresia of the esophagus with tracheoesophageal fistula, with fistula between (a) the upper segment and the trachea, (b) the lower segment and the trachea or a bronchus (91 per cent of the cases according to Haight<sup>1</sup>) and (c) both segments and the air passages

A fourth type, in which there is tracheoesophageal fistula without atresia, was reported by Haight<sup>1</sup> to have been seen in 3 per cent of his combined series of cases.

In a case of suspected tracheoesophageal fistula without atresia, the roentgenologic diagnosis may not be apparent if the examination is carried out with the patient in the supine position. The importance of roentgenologic examination with the patient in the prone position in these cases has been stressed by Holt, Haight, and Hodges.<sup>2</sup> The prone position causes the fistula to be dependent in its relation to the esophagus, thereby allowing the iodized oil to enter the trachea by gravitation.

### SUMMARY

Congenital tracheoesophageal fistula without an associated atresia of the esophagus is of rare occurrence. It has been observed in approximately 3 per cent of the cases of congenital esophageal anomalies. The diagnosis may not be apparent on roentgen examination with a contrast medium, unless examination is carried out with the patient in the prone position. The case of a newborn infant in whom a tracheoesophageal fistula was suspected, and demonstrated by roentgenograms and repaired successfully on the fourth day of life is presented.

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## A HOSPITAL SPECIAL CARE UNIT

A speci l c e unit is a seg gated hospit l area in wh ch  
cutely ill p tients r conc ntrat d Th unit is spec ally  
equipped has an augmented local supply and an augm nt d  
staff The function of such unit is to provide special  
ntensive nd exp rt care for the acutely ill Such a unit  
has been in oper ti n t the Hitchcock Hosp tal in H n ver  
New Hampshire for the past two ye rs nd h s p oven a  
valuable asset for the medical staff the nurses and the  
patient The re n for stablish ng such a unit are many  
P imary s th p oblem of the incre sing number of acutely  
ill in our hospit ls Advance in medical and surgical treat  
ment re producing patients requiring sp cial tention nd  
preserving pat ents heretofore beyond s lvage These pa  
tients need tensi e nursing care yet the supply of nurse  
is hort and unable to cope with the ever i creasing load  
It i bvious that mo e efficient utilizat on of pers nnel and  
concentrat on of effort is essent al if we are to fulfill our  
obligations to the cut ly ill pat ents

—WILLIAM T MOSENTHAL M D

J m l f th M M d l A t  
p 396 N 1957

# Lipoma of the Oral Cavity

BYRON G McKIBBEN *Colonel MC USA*

WALTER B EIDBO *Captain MC, USA*

**L**IPOMAS may occur wherever fatty tissue is found, and occasionally are seen in the oral cavity<sup>1</sup> In this location, they generally arise from the fat cells in the gingiva, or from adipose tissue in the buccal space, tongue, or floor of the mouth Congenital lipomas of the cheek have been reported<sup>2</sup> While deep seated lipomas in other parts of the body have been known to undergo malignant change, those in the oral cavity apparently always remain benign<sup>3</sup>

Lipomas are well defined, soft tumors and produce no symptoms other than those due to their mass They may be pedunculated or sessile, may be rounded or have variable formations with several lobes, and have been found bilateral They are not resorbed like natural fat stores, which are removed when the person loses weight<sup>4</sup>

In 1934, Geschickter<sup>3</sup> reported on a series of 622 lipoid tumors recorded in the files of the Surgical Pathological Laboratories of Johns Hopkins Hospital His analysis showed that 460 of these tumors were benign lipomas, and that only three of them were located in the oral cavity

At the Armed Forces Institute of Pathology during the five year period, 1953 to 1958, 1 768 primary tumors were recorded in the Registry of Oral Pathology These were all types, both benign and malignant Of the 1 768 tumors 17 (less than 1 per cent) were lipomas<sup>5</sup>

## CASE REPORT

A 38 year-old Negro woman was first seen in the ear nose and throat clinic of this hospital 21 November 1957 because of a mass in the right cheek She stated that she had first noticed the mass four months previously and that it had increased slightly in size

On physical examination a discrete soft nontender freely movable mass measuring about 4 cm in its greatest diameter was palpated in the right cheek lateral to the mandible The tumor caused the right

From William B. United Army Hospital El Paso Texas



cheek to bulge about 1 cm and with the mouth open the buccal surface also was seen to bulge. The neck was free of palpable nodes.

The patient was admitted to the hospital 10 January 1958 and under anesthesia with 1 per cent infiltration of Xylocaine Hydrochloride (brand of lidocaine hydrochloride) an incision was made through the buccal mucous membrane and the tumor—which was well encapsulated—was easily shelled out by blunt dissection. The fibrous capsule of the tumor appeared to be continuous with the fascia along the lateral side of the mandible. A rubber drain was inserted and the wound was closed with No. 0000 plain gut sutures.

The gross specimen was somewhat egg-shaped and measured 4 by 2.5 by 1.5 cm. The external surface was smooth, yellow in color, and was covered with a thin fibrous capsule. The cut surface was yellow, gray, lobulated, and had the appearance of adipose tissue (fig. 1).

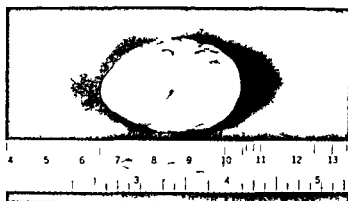


Fig. 1. Appearance of the gross specimen.

Microscopic examination showed lobules of benign adult fat cells. A network of connective tissue separated the lobules and formed the capsule. Benign vascular structures were seen throughout the tumor mass (fig. 2).

**Comment.** It is interesting to note that a tumor of this size located in the cheek was not observed by the patient until 4 months prior to the time when she first sought medical attention. Lipomas are known to be slow growing, and this one must have been large enough to cause a noticeable bulge and to be palpated for well over a year prior to the time of its detection by the patient.

#### SUMMARY

Lipomas of the oral cavity are not common. They are slow growing and benign and produce no symptoms other than those due to their mass. One case in a Negro woman is presented.



Figure 2. Photomicrograph showing connective tissue capsule to the left. Adult adipose cells are seen in the remainder of the section. ( $\times 35$ )

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#### WHY SEAT BELTS?

No single safety device has been more effective in a crashing auto than the properly installed seat belt. On this the experts agree especially in a market of high speed power brakes and trigger-happy driver feet.\*

—MEDICINE AT WORK  
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# Thymoma and Myasthenia Gravis

HAROLD COLLINGS J M ; MC USA  
WILLIAM R SWEETMAN M J MC USAR

**T**HE association of thymoma and myasthenia gravis has been known since 1901. Sixteen per cent of a large series of patients with myasthenia gravis were found to have thymomas. As many as 75 per cent of patients with thymoma have had associated myasthenia gravis.

The causal relationship between thymoma and myasthenia gravis is not certain. The fact that myasthenia gravis may develop several years after the diagnosis of thymoma makes it unlikely that the thymoma is caused by the myasthenia gravis. That the thymoma causes the myasthenia gravis is an attractive possibility which is supported in many cases by remission or marked improvement of the disease following treatment of the thymoma. Some experimental evidence has been obtained that extracts of fetal whale thymus and of human thymomas have a myasthenia gravis like effect on nerve muscle preparations and on animals. However reports of cases in which myasthenia gravis developed after the removal of thymomas<sup>1-6</sup> have raised doubts that thymomas cause myasthenia gravis. The development of myasthenia gravis during the early postoperative period in some of these cases is not convincing evidence against such a causal relationship. In spite of apparently complete removal of a thymoma there may be recurrence of thymoma<sup>7</sup> and in only one of these reported cases of myasthenia gravis developing after the postoperative period has there been autopsy evidence that no recurrent tumor was present (In that case there were some hyperplastic thymus remnants.) These reports of myasthenia gravis developing after surgical removal of a thymoma do not disprove the idea that thymomas may cause myasthenia gravis. That both thymoma and myasthenia gravis are caused by a third unknown factor is a possibility.

The myasthenia gravis associated with thymoma usually is rapidly progressive and severe treatment is a difficult problem. Such cases are relatively rare and all should be reported so that eventually some conclusions may be drawn regarding proper management. Since 1947 two patients with thymoma and myas

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S yr P

thenia gravis have been seen at this hospital. The first case is taken from the hospital records, the second patient was seen and treated by the authors.

### CASE REPORTS

**Case 1** A 51-year-old man had been completely asymptomatic but was transferred to this hospital on 31 March 1947 because of the finding of a mediastinal mass on a routine chest roentgenogram. Past history was not significant except for congenital syphilis which had been treated with bismuth arsenicals, and artificial fever.

Physical examination was not remarkable. Roentgenograms of the chest revealed a sharply circumscribed tumor mass extending laterally and anteriorly from the left hilar region (figs 1 and 2).

On 16 April a left thoracotomy was performed and a tumor was found in the anterior mediastinum just anterior to and above the arch of the aorta. The tumor was very densely adherent to the pericardium and could not be removed. Microscopic examination of the biopsy specimen revealed that it was a thymoma.

The postoperative course was uneventful and from 29 April to 23 May 1947 the patient received 2,200 r of radiation to each of two fields over the mid chest anteriorly and posteriorly.

The patient was last seen at this hospital 2 July 1948 at which time he was asymptomatic and demonstrated no evidence of myasthenia gravis.

A letter dated 30 May 1949 stated that the patient recently had developed severe myasthenia gravis requiring large doses of Prostigmin (brand of neostigmine). Subsequent correspondence related that the patient died 9 June 1949 of respiratory paralysis, myasthenia gravis, and tumor of the thymus.

**Case 2.** A 39-year-old woman was admitted to this hospital for the first time on 4 October 1955. In August she had noted inability to chew and a month later difficulty in swallowing. She had also noted difficulty in talking and weakness of her extremities. Activity increased all symptoms. After noting drooping of the left eyelid and vertical diplopia she was hospitalized at another hospital where a neostigmine test was positive for myasthenia gravis. She was started on small doses of neostigmine and transferred to this hospital. Examination revealed ptosis, vertical diplopia, severe weakness of masticator muscles, nasal voice, marked weakness of neck muscles, moderate weakness of muscles in the upper extremities, most marked in proximal muscles, and some weakness of hip girdle muscles. Radioactive iodine uptake studies revealed no evidence of hyperthyroidism. A postero-anterior roentgenogram of the chest was normal. Gradually increased neostigmine dosage resulted in decreasing muscle weakness so that by 29 October the patient was fairly well controlled on daily intake of 33 tablets (15 mg per tablet) of neostigmine and was discharged from the hospital.

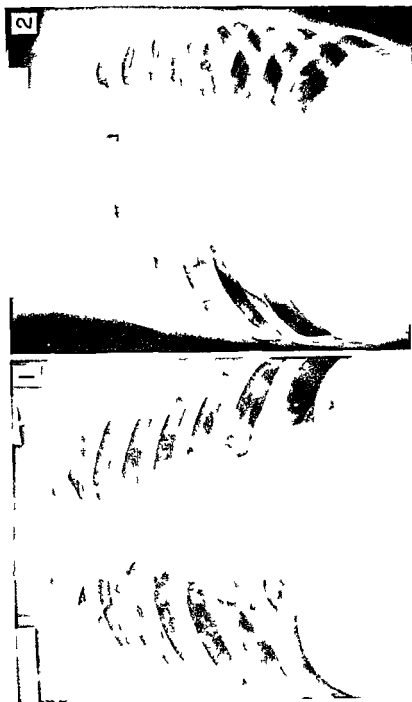


Fig 1 d 2 ( as 1) R ig gam fth b t bou g t m mas xt d gat ly and l t ally from th l ft  
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The patient was admitted to this hospital for the second time on 22 May 1956 with the history that her weakness had rapidly increased in spite of taking 30 tablets of neostigmine and 22 tablets (60 mg per tablet) of Mestinon (brand of pyridostigmin bromide) daily. She had been very weak most of the time and had had at least two episodes of acute respiratory distress. Roentgenograms (including a lateral view) of the chest revealed a nodular anterior mediastinal mass in the region of the ascending aorta (figs 3 and 4).

On 26 May the patient had the onset of progressive respiratory distress so that after several minutes respirations were minimal and cyanosis was present. The administration of Tensilon Chloride (brand of edrophonium) intravenously produced dramatic improvement in her condition which was maintained with neostigmine administered intramuscularly. Oral medication was gradually increased to a total of 63 tablets of neostigmine and of Mestinon each day.

From 7 June to 14 July the patient was given irradiation therapy with a total dose of 3 994 r to the mediastinal tumor. During this time her neostigmine requirements decreased to 40 tablets daily. Roentgen studies indicated that the mediastinal mass had decreased about 50 per cent in size. The patient was discharged from the hospital for three weeks prior to surgery. By the time of the third admission on 14 August 1956 her neostigmine requirements had decreased to 26 tablets daily.

On 22 August a right thoracotomy was performed under gas-oxygen-ether and Pentothal (brand of thiopental sodium) anesthesia. A lobulated egg shaped firm movable tumor mass measuring 8 by 5 by 7 cm was found in the anterosuperior mediastinum overlying the arch of the aorta. It was adherent to the pericardium but seemed to be entirely encapsulated. The tumor was totally removed. Following thoracotomy a tracheotomy was performed as a precautionary measure in the management of myasthenia during her postoperative period.

The patient was not given neostigmine on the morning of surgery but was given 1.5 mg intramuscularly at the completion of the operation. She was observed carefully but required no more for some 18 hours, at which time increasing weakness and apprehension appeared. She received 1 mg of neostigmine intramuscularly every two or three hours for the next week. One week postoperatively oral medication was resumed. On 22 tablets of neostigmine daily muscular twitching occurred and that medication was gradually decreased to 15 tablets daily by 8 September.

The patient was discharged from the hospital 26 September and returned to her factory job in October 1956. When last seen on 23 April 1957, she no longer took neostigmine regularly (although once every few days she took 1/4 of 1 tablet) and had been asymptomatic. Examination at that time revealed only mild weakness of shoulder girdle muscles. Roentgenographic examination of the chest showed no recurrence of tumor. In April 1958 the patient wrote that she was doing well and was taking from 1 to 3 tablets of neostigmine each day.



Figures 1 and 2 (as 1) R t g am f the b t show g at m mas ste d g t r i y a d l t ally from th l ft  
b l e g n.

## DISCUSSION

The prognosis in patients with myasthenia gravis and untreated thymoma is very poor. Either the myasthenia gravis or the untreated thymoma represents sooner or later a serious threat to life.

Although it is generally agreed that thymectomy is of value in the treatment of progressively severe, generalized myasthenia gravis in young women without thymomas, results with surgical removal of thymomas in the presence of myasthenia gravis without prior irradiation therapy have been uniformly bad. Of nine such patients reported by Grob<sup>8</sup> from the Johns Hopkins Hospital, six died of myasthenia gravis. Schwab and Leland,<sup>9</sup> in reporting the series from the Massachusetts General Hospital, concluded that the results were no better with surgical intervention than without it. In the series of 39 patients with surgical treatment of thymoma reported by Eaton and Clagett<sup>1</sup> from the Mayo Clinic, there were 5 operative deaths and 14 subsequent deaths (all but one of myasthenia gravis); in only 13 was there symptomatic improvement. In a total of 11 patients reported by Keynes<sup>10</sup> in whom surgical treatment was undertaken without previous irradiation therapy, there were 3 operative deaths. Only 3 patients were living after two years, and only 1 was living at the time of Keynes' report.

No large series of patients treated only with irradiation therapy has been reported. Some reported cases, however, suggest that it does frequently bring about an improvement in the myasthenia gravis and the tumor.<sup>1</sup> In some reported cases, it seems likely that irradiation therapy of the thymoma delayed the onset of myasthenia gravis. This perhaps was true in case 1.

Although Keynes' results in the early patients treated only with thymectomy were very poor, the results were much better in 21 cases treated first with irradiation therapy followed by surgical intervention.<sup>10</sup> Four patients were well up to five years after surgery; 8 were much improved; 1 was unchanged; and 5 patients died. The results thus were gratifying in 12 out of 21 patients. It is possible that the development of improved surgical and anesthetic techniques and more experience in the medical management of myasthenia gravis partially account for the difference in results in Keynes' two series of patients. It seems most likely, however, that irradiation therapy was at least partially responsible for the better results.

Every patient with myasthenia gravis should have roentgenographic examination (including lateral or oblique views) of the chest for evidence of thymoma. If such is found, it is believed the tumor should be treated with irradiation therapy, followed by surgical removal of the tumor if such is possible. Careful medical management of the myasthenia gravis during and after treatment of the tumor is mandatory.



## SUMMARY

The relationship between thymomas and myasthenia gravis has been reviewed. Every patient with myasthenia gravis should have a roentgenographic examination of the chest including lateral or oblique views for evidence of a thymoma.

Management of associated thymoma and myasthenia gravis is a difficult problem. The results have been best in patients treated with irradiation therapy followed by surgical removal of the thymoma.

Two cases with thymoma and myasthenia gravis have been seen at this hospital since 1947. One patient died of myasthenia gravis two years after irradiation therapy for an inoperable thymoma. In the other case treatment of the thymoma by irradiation therapy followed by surgical removal resulted in almost complete remission of the myasthenia gravis.

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# SERVICE ARTICLE

## EFFECTS OF HIGH INTENSITY NOISE ON NAVAL PERSONNEL

HALLOWELL DAVIS M D

**B**EGINNING in 1952, several studies were made of the effects on naval personnel of the operation of jet airplanes from the decks of aircraft carriers, because questions had arisen as to what effect the exposure to high intensity noise would have on the flight deck personnel. In 1953 a broad, exploratory study, now known as the BENOX study, was made of the biological effects of noise on man. The BENOX Report,<sup>1</sup> was reviewed and commented upon by the then newly formed Armed Forces National Research Council Committee on Hearing and Bio-Acoustics (CHABA),<sup>2</sup> and recommendations were developed for research in this area. Both the BENOX Report and the CHABA commentary expressed the fear that exposure to jet engine noise in the unexplored range above 140 decibels might actually be producing injurious cumulative aftereffects. The Auditory and Non Auditory Effects of High Intensity Noise (ANEHIN) Project\* was organized in April 1954 to study the problem that was stated so clearly in the above mentioned reports.

### NATURE OF THE PROGRAM

The project was conceived and planned as a field study, first to identify and thereby protect those individuals who might actually be suffering injurious effects, and second because it seemed impossible to bring into the laboratory both the noise exposures and the other stresses of actual military duty that

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Presented at the Fifth Annual Meeting of the Armed Forces National Research Council Committee on Hearing and Bio-Acoustics: Washington, D. C., 29-30 October 1957. This presentation was supported by Contract Number 1151 (01) between the Committee and the Department of the Navy, Naval Research Laboratory.

Director: Dr. S. Durrant of the Research and Development Division of the Department of the Navy, Naval Research Laboratory. Also is Director of the Auditory and Non Auditory Effects of High Intensity Noise Project: Dr. Robert W. B. (Physicist and Electrical Engineer) and Mr. Arthur Nemoiler (Research Assistant).

The work has been performed by the Central Institute for the Department of the Navy, Naval Research Laboratory, School of Aviation Medicine, Philadelphia, under contract Number 1151 (02) with the Office of Naval Research, Central Institute for the Department of the Navy, Naval Research Laboratory. Principal participating major service to the contract were the Thor (Principal Director), Dr. W. D. Ward (Experimental Psychologist), Dr. D. D. G. Durrant (Experimental Psychologist), Dr. Robert W. B. (Physicist and Electrical Engineer), and Mr. Arthur Nemoiler (Research Assistant).

might combine with noise to produce aftereffects such as chronic anxiety or undue fatigue. The location selected for the field study was the flight deck of aircraft carriers where the personnel forward of the island are exposed to particularly high noise levels. The study later was extended to include land based maintenance personnel who serviced high performance jet powered aircraft. These two categories suffer the most severe sustained noise exposures regularly encountered in line of military duty.

### Program Objectives

Except for the familiar impairment of hearing for high frequency sounds, the nature of the cumulative ill effects that were sought by the ANEHIN Project was not known in advance. The only clear specification was to look for undesirable *cumulative aftereffects*. It was never part of the ANEHIN objective to study the impairment of performance that may occur *during* noise exposure. This was conceived as a separate problem that might well be attacked as a laboratory experiment rather than as a field study. In other words, the ANEHIN Project was a wide spreading trouble hunt in which the testing "net" was designed to cover as many aspects as possible. For this reason, a large variety of tests and procedures in addition to audiometry were employed to detect possible changes in sensory and psychomotor performance equilibrium, central nervous and complex intellectual functions, anxiety, motivation, and the incidence of sick calls and accidents.

In planning the project, the inclusion of physiologic indicators of stress also was considered very carefully, particularly those that involve the activity of the adrenal gland together with certain recognized medical indicators such as might be revealed by complete neurologic examinations. Another area of possible test and study was social and group behavior. Such studies were deferred although not rejected outright, because of the elaborate and expensive nature of some of the procedures that would have been involved on the one hand and because in the case of the physiologic indicators it soon appeared that the degree of stress involved in the actual noise exposures was insufficient to create any real probability of obtaining positive results.

The ANEHIN Project actually became more than a search for the effects of high intensity noise. It became a prototype of a very similar trouble hunt that might be indicated at a later time in relation to any other new stress that may be created for personnel by future developments in the weapons and operations of modern warfare. The ANEHIN effort to carry out such a trouble hunt in the form of a field study has revealed certain difficulties and limitations inherent in any field study which in spite of the consistently fine co-operation that the project received both afloat and on shore seriously limited the scope and the significance of its actual findings. Field studies have their place, but they are expensive and time consuming, and the un-

avoidable limitations imposed by operational considerations may seriously impair the scientific value of the entire effort

## ANEHIN CONTRIBUTIONS TO FUTURE RESEARCH

### Test Batteries

As a positive contribution to any subsequent trouble hunt, the ANEHIN Project leaves a battery of physiologic, psychologic, and psychomotor tests and a group of questionnaires and pencil and paper tests of proved practicality and reliability. Significant progress was made toward the development of a standardized psychiatric interview and a rating scale based on the information so obtained. The tests cover a wide variety of functions and behavior. So wide is this variety that, in spite of the obvious holes in any system of screening, we believe that the probability of detecting undesired cumulative aftereffects of any sort is actually very high. Of course, in any other application, such as to the problems of vibration which may soon beset us in the future, special tests of any particular motor, sensory, or medical function that may be obviously endangered or already definitely implicated would be substituted for the audiometry that was emphasized in the ANEHIN Project.

### New Test Equipment

As tools to be used in the search for cumulative aftereffects of high intensity noise, a mobile laboratory and two new instruments were developed. All three may have a fairly wide application and significance in future work in this area.

1 *The mobile laboratory* A mobile laboratory was developed to house the audiometric, the physiologic, and the psychologic apparatus, and to provide the proper environment for such tests in the field. In our trailer mounted, sound treated laboratory\* (fig 1), it was possible to make satisfactory audiometric measurements and to conduct psychophysiologic tests on the hangar deck of an aircraft carrier during training operations at sea. To provide adequate acoustic environment for audiometric testing in such a situation was no mean accomplishment from the point of view of acoustic engineering.

2 *The group audiometer* One of the new instruments developed for this study is a group audiometer that employs the psychophysical method of single descent.<sup>4</sup> This instrument is designed to test 10 subjects at a time. It is semiautomatic, and in its full and final form includes an automatic print out device that prints immediately the hearing losses of the 10 subjects in 10 type written columns (fig 2). Audiograms for both ears of 10 men can be obtained in from 10 to 15 minutes. Fortunately, and somewhat unexpectedly, the method of single descent as incorporated in this audiometer has proved not only reliable but valid. The actual threshold values agree closely enough with the threshold values

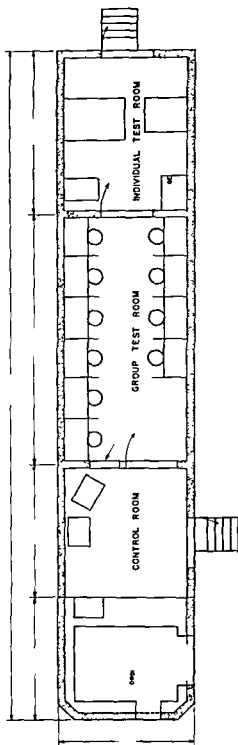


Figure 1. Floor plan of the mobile laboratory for auditory and motor testing. The laboratory has a total area of 10 m x 10 m and is a mobile unit.

determined by the accepted standard methods of clinical audiometry to make it legitimate to consider the ANEHIN Group Audiometer for routine use in monitoring audiometry Further

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250 L	3 32	00 00	34 36	44 42	28 28	40 38	44 40	00 00	32 34	30 36
500 R	48 48	00 00	56 58	54 54	44 46	54 54	62 64	00 00	46 50	56 56
500 L	50 48	00 00	46 48	68 66	46 40	56 54	58 56	00 00	42 50	56 56
1000 R	54 54	00 00	62 70	74 76	50 44	60 62	64 68	00 00	56 58	64 66
1000 L	52 52	00 00	64 66	64 78	50 42	60 60	64 68	00 00	60 56	64 62
2000 R	58 58 60	00 00 00	58 58 60	90 72 70	52 56 54	64 58 64	76 70 72	00 00 00	66 62 58	66 64 62
2000 L	60 52	00 00	64 58	76 68	56 46	50 52	70 70	00 00	60 44	62 54
4000 R	40 42	00 00	62 60	78 80	44 40	44 58	70 72	00 00	58 62	60 60
4000 L	36 38	00 00	58 58	68 70	42 46	44 50	58 64	00 00	56 70	56 56
8000 R	00 00	00 00	26 20	54 52	00 00	50 48	42 44	00 00	46 46	48 52
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4	JIC									
5	JDH									
6	LNR									
7	WG									
8	Unoccupi d									
9	WM									
10	RVP									

Figure 2 Sample data sheet from the Automatic Audiometric Data System (AADS) The two-digit numbers in the 10 columns are typed automatically. The operator makes all other entries. Readings are in thresholds expressed in decibels of attenuation below the starting level of the test tone. Returns at each frequency demonstrate the repeatability of the procedure. Note that the occupant of Station 4 failed to push his Don't Hear button on the first trial of 2000 cycles per second in the right ear resulting in a reading of "90". The operator chose to repeat the test a third time at this frequency to verify the readings obtained on the second trial.

trial of the method with this end in view is being carried out at the U S Naval School of Aviation Medicine Pensacola, Fla

3 *The noise cumulator* The second instrument developed for this study is called a noise cumulator It is designed to measure the actual noise exposures incurred by personnel during military operations It gives numerical measures of noise exposure in terms of the total duration of exposure to noise in specified frequency bands and above various preset intensity levels The field use of the instrument involves tape recording the noise exposure experienced by a man during the actual performance of his job This is accomplished by means of a frequency modulated short wave transmitter worn in the man's helmet which broadcasts to the tape recorder those noises actually experienced at the wearer's head Analysis of the tape recording is carried out later in the laboratory The field unit, including microphone and transmitter performs reliably and accurately in noise fields up to 150 db The noise cumulator was used successfully on board the U S S *Forrestal* Considerable experimental work must still be done however to validate the measures obtained in terms of specified biological effects Several different bases of acoustic analysis can be employed depending on the choice of the method of rectification of the signal the frequency bands and the spacing of the intervals of intensity Unfortunately impulse type noises such as gunfire are still beyond the scope of the instrument The particular measure or form of analysis must be found that correlates best with some specified effect This will be a long and difficult task, but in the meantime the noise cumulator is already suitable for a basic survey of the actual current noise exposures that are associated with the operation of various aircraft and many other types of noisy equipment If routine noise studies of the operation of new equipment are also carried out any great increase in the noise exposure of service personnel can be detected or forecast in advance of actual field use

#### THE ANEHIN FIELD STUDIES OF NAVAL PERSONNEL

During the years 1955 and 1956 many brief studies were conducted at the U S Naval School of Aviation Medicine to perfect the group audiometer and the various methods for psychologic physiologic and psychiatric testing Considerable attention was devoted to the selection of tests suitable for use in the mobile laboratory under field conditions and to the collection of normative data It was part of the original concept that a second laboratory at the U S Naval School of Aviation Medicine should also be maintained to develop new methods and to apply them to samples of naval personnel and this type of work continues Three field studies were successfully conducted

### The Ticonderoga Study

The first field study was carried out on board the U S S *Ticonderoga* in two sessions, one during September-October 1955, and the other in May-June 1956. In 1955, preliminary sea trials were made using the mobile trailer laboratory. Audiometric measurements were made, and the various psychologic tests were tried out. In 1956, our psychiatrist colleagues, Capt Philip B Phillips, MC, USN, and Lt William I Stryker, MC, USNR, joined the ship in Istanbul, Turkey, at a time when the *Ticonderoga* had been operating in the Mediterranean for a period of 7 1/2 months. They administered questionnaires to and conducted standardized psychiatric interviews with a group of 70 selected personnel who had varying degrees of noise exposure in their different jobs. No definitive audiometric measurements or laboratory tests were conducted in connection with this second section of the study.

### The "Forrestal" Study

The second study was carried out on board the U S S *Forrestal* during its January-March 1956 training operations. In this study the feasibility of performing audiometry on board an aircraft carrier and also of measuring the noise exposure of personnel during operations by means of the noise cumulator was demonstrated. Psychologic and psychiatric tests were also successfully performed. This field study was more important as a demonstration of methods and their potentialities than as a source of definitive data, but the data and the qualitative impressions are all in agreement with those based on the two other studies.

### The Cecil Field Study

Definitive studies of hearing and of psychologic performance were conducted in a third field study at U S Naval Air Station, Cecil Field, Fla., during the late summer of 1956 and early spring of 1957. The personnel selected for study in this case were chiefly maintenance personnel attached to various aircraft squadrons. The entire battery of tests, including audiometry, was employed in the summer of 1956 and then again after a period of approximately six months as a before and after study. The personnel included those who, by the nature of their jobs and the equipment with which they were associated, seemed to be the naval personnel incurring at this time the most severe noise exposures in terms of both intensity and duration. Control groups were selected from personnel who were not routinely exposed to jet noise.



## LIMITATIONS OF THE ANEHIN STUDIES

## Field Limitatio

First, the ANEHIN study was a *field* study. The great advantage of a field study is that the results obtained are valid for the actual practical situation, but for this very reason it is more difficult to extract from the data any general statements or exact numbers. There are too many uncontrolled variables and extraneous factors, too much attrition of the original group in a test-retest study, and too little control of the major stimulus itself—in this case the noise exposure.

## Measurement of Noise Exposure

A second limitation is that there is no accepted, satisfactory measure of noise exposure. The noise exposures of flight deck and flight line maintenance personnel are brief exposures to noise of high but often rapidly changing intensity. The relations between intensity and duration for a given biological effect are unknown, and until the noise cumulator is employed the actual intensities and durations of operational exposures will not be known with any degree of precision. The independent variable noise exposure is therefore so vague that we cannot yet draw precise conclusions even when the dependent variable is measured numerically as decibels of threshold shift or as scores on well standardized psychologic or physiologic tests. It was for just this reason to define the noise exposures numerically that the development of the noise cumulator was made a primary part of the project, but that development is only just now complete and the present conclusions suffer accordingly in generality and in precision. We have been forced to rely on estimates of noise exposure based on questionnaires and on grouping men according to their jobs and according to the equipment used. We could do little more than give a rank order to the noise exposures of various groups as "high," "moderate," or "low," and sometimes only "more" or "less."

## Neuropsychiatric Evaluation

Finally, in the area of neuropsychiatric evaluation the situation was even worse because a neurologist's or psychiatrist's clinical judgment is a subjective opinion based on many facts of observation and much previous experience. And it was to just this area of motivation, anxiety, fatigue, et cetera that most of the anecdotal evidence of the BENOX Report pointed as the likeliest place where undesirable nonauditory cumulative aftereffects might be found. We therefore undertook to develop better methods of observation and evaluation, first by systematically standardizing the psychiatric interviews so that the same areas would be explored in all cases, and second by developing a psychiatric rating scale to make the evaluation of

the information more objective and reliable. This development is still incomplete, however, and, like the noise cumulator, it must still be validated. For the present, then, although the results obtained with the psychiatric rating scale are given in the full U S Naval School of Aviation Medicine Report, we still were forced to rely largely on the clinical impressions and judgments of our two psychiatrists. Fortunately, both of them were naval officers, and, therefore, had a background of appropriate clinical experience.

### CONCLUSIONS AND RECOMMENDATIONS

Because of the limitations mentioned above, our results are neither all yes and no, nor sharply black or white. There are large gray zones of uncertainty in between, and because we cannot say "yes" it does not mean that the answer is necessarily "no." We do have at least partial answers to the following practical questions:

- 1 Should present operational procedures be modified, or are new types of protective equipment required, to protect military personnel from the cumulative ill effects of present noise exposures?
- 2 Are the new criteria for hazardous noise exposure too lenient? Are they too strict?
- 3 What of the future, with its expected increase in the noise levels of jet engines and other noise sources?
- 4 What recommendations emerge for the protection of personnel and for further study?

With practical questions, a precise scientific statement of fact does not constitute a complete answer. In addition, some kind of value judgment is involved or some extrapolation into the unknown is expected. The scientific data that we have, with our statistical analyses, will appear in a report to be issued by the U S Naval School of Aviation Medicine. The collective judgments of the ANEHIN group on the practical questions listed above, and a brief statement of the kind of data upon which each judgment is based, are as follows:

As of March 1957 there was no reasonable cause for immediate alarm concerning cumulative ill effects from the operational exposure of personnel to jet engine noise. We see no present need for changes in operational procedures or for protective equipment other than ear protectors of types that are currently available.

We have no evidence that the criteria of 1957 for hazardous noise exposures should be made more strict, nor can we say with assurance that they are too lenient. They lie within the zone of uncertainty of our conclusions.

Some of our findings suggest but do not prove that present operational exposures to jet engine noise may be near the limit of producing permanent impairment of hearing and also a general impairment of performance on a wide variety of psychologic tests. With increased noise exposure these effects may become not only clearly measurable but also of practical medical or operational significance. Efforts should therefore be continued to establish clearly the limits of tolerance for noise exposure by (a) controlled laboratory experiments with volunteer subjects (b) continued monitoring of actual operational noise exposures (c) routine monitoring audiometry for all seriously noise exposed personnel (d) monitoring by selected psychologic tests of sample groups of the personnel who incur the most severe noise exposures and (e) continual alertness of military medical officers to psychiatric or other medical indications of increased stress either general or specific associated with habitual noise exposure.

The most urgent research need is to develop a valid measure of noise exposure such as the noise cumulator may provide, and to apply it to men during operational procedures with current and also with future noisy military equipment.

If adequate measures of actual and expected noise exposures are made and if routine monitoring audiometry and also small sample psychologic and physiologic monitoring of highly noise-exposed personnel are instituted, then it will be legitimate to transfer some research effort from the problem of possible cumulative ill effects of noise exposure to the more urgent problems of the impairment of performance including communication, in the actual presence of intense noise.

If and when a substantial increase in noise exposure occurs, due either to the introduction of noisier equipment or a change in operational procedure a new study of cumulative effects should be undertaken by methods similar to those used in the present study.

## ANALYSIS OF OBSERVATIONS

### Noise Measurement

Measurements of the noise exposure experienced by several members of a flight deck crew were made aboard the U S S *Forrestal* in March 1956. These preliminary measurements were concentrated on two members of the flight deck crew whose duties were such that they apparently were exposed to more intense noise than others. The measurements were accomplished by means of a miniature frequency modulation (FM) transmitter worn by the observer, an FM antenna on the flight deck next to the catwalk, and a fixed FM receiver and tape recorder located below deck. Figure 3 shows a record of the exposure of the forward plane director during a typical launch.

Cumulative distributions of noise level versus exposure time were obtained from a specially designed instrument, the noise cumulator. Operational exposures to very high intensity noise

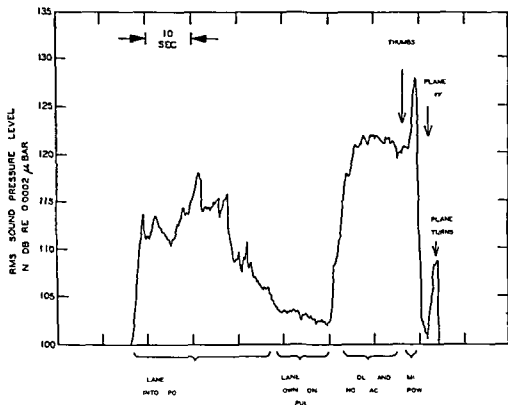


Figure 3 Over all sound pressure level to which the forward plane director is exposed during a typical launch. The aircraft is the F7U 3 without operation of the afterburner.

are extremely brief (fig. 4) The duties of one of the men studied, the forward plane director, placed him in the center of the deck 20 to 50 feet behind the catapults. The second man studied was responsible for attaching the holdback mechanism to the rear of the airplane on the catapult. Both men appeared to spend more time than any others in the high intensity regions of the sound field behind jets. However, neither man experienced peak levels in excess of 138 db for more than about 3 seconds during an average launch. As many as 100 launches in a day would produce less than 5 minutes total exposure to such levels. Even exposure to peak levels above 115 db would total less than 1 1/2 hours daily.

This exposure to noise is significantly less than had been assumed in considerations of the possible hazards associated with noise exposure aboard aircraft carriers. The brevity and infrequency of exposure to extremely high noise levels has a very important effect on the noise exposure. This effect can be demonstrated by estimates of the equivalent steady exposure

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August 1956 audiograms were obtained on 1,200 Navy enlisted men who were normal by otologic examination, including 579 men with some history of regular exposure to jet engine noise, and 379 with little or none. Among the latter were 91 men under 25 years of age who had not been exposed to large caliber gun fire. These 91 men served as a "biological baseline." Their hearing was similar to that of similar groups in previous survey studies. In the initial audiograms, hearing losses were slightly greater among those men who were, or who had been, exposed to noise from reciprocating engines or from jets without afterburner. It is not certain from this cross section study, however, that the engine noises had produced these hearing losses. Another probable cause of the greater hearing losses was gun fire. Almost twice as many of the "noise exposed" personnel in the age groups 17 to 22 and 23 to 28 years had been subjected to large caliber gunfire. They also reported more tinnitus following their exposure to gunfire. The greater tinnitus suggested that, on the average, the severity of noise exposure may have been significantly greater for this group than for the "non noise exposed" group.

More significant than these moderate initial losses, however, are the follow up audiograms taken of 220 of these same men in squadrons that were flying jet planes with afterburners. These were the men who presumably received the most severe noise exposures in the interval, yet they showed on the average *no additional hearing loss after seven months of routine activity*. A similar negative result also was found in our study of flight deck personnel during a three months' training cruise aboard the U S S *Forrestal* in 1956.

The results of audiometric study at Cecil Field are presented and analyzed in considerable detail in an article by Ward.<sup>5</sup> Here the possible complications resulting from temporary threshold shift and from some increase in the use of protective equipment are considered carefully. A small additional impairment of hearing may have occurred during the seven months of noise exposure, but if so it was obscured by these factors that could not be controlled. The possibility that the men with initially greater hearing losses might be those who are more susceptible to incurring additional hearing loss from additional exposure also was examined, but no indication was found that men with pre existing losses are more likely to suffer additional losses than men with normal hearing.

Obviously, the negative results of this study of men before and after seven months of routine operational exposure to jet engine noise is most reassuring. The results should not be interpreted, however, as contradicting in any way the criteria that have been established by other groups for hazardous noise exposure, particularly for exposure to steady industrial noises.

The criteria were developed on the basis of many years of noise exposure while the present study extended for only seven months. The number of men who could be studied before and after this seven month period under comparable conditions is not very large and the expected slight trend toward increased hearing losses may be obscured by the many other factors that were involved. It is worth noting however that negative results very similar to the present ones have been obtained in other studies in which men exposed to aircraft noise have been monitored over a period of time. Sataloff,<sup>6</sup> in a five year study of men working around jet engine test cells, found only slight changes and even these could not be attributed unequivocally to noise. Similar negative results recently were reported by Kopra<sup>7</sup> in a study of Air Force personnel.

### **Nonauditory Effects**

The search for nonauditory effects was also largely negative. In the preliminary studies aboard the U S S *Ticonderoga* and the U S S *Forrestal* no large differences were found between groups of noise exposed and non noise exposed subjects. The final study at Cecil Field consisted of three parts. First a group of 16 psychologic tests was administered twice to the same personnel with an interval of six months between tests. Second sick call records were analyzed according to total frequency of reports to sick call. Third a group of nine paper and pencil tests was given during the final testing period.

The battery of psychologic tests had been selected in order to sample as widely as possible a variety of different sensory, psychomotor and intellectual functions. Twenty five tests were employed in all: critical flicker frequency, tapping speed, reaction time, fine hand steadiness, gross hand steadiness, standing steadiness and Knox Cube Test, fine dexterity, the Digit Symbol Test, tests of visual acuity, phoria and depth perception, the Cornell Index, the Saslow Screening Inventory, the Taylor Anxiety Scale and in addition nine factored aptitude tests that were given only at the end of the six month period.

Analysis of the results of the initial tests given at Cecil Field in August 1956 showed no large differences between men having a history of exposure to jet noise and those having had no previous noise exposure. Our primary interest however was in assessing changes in test performance following the six month period between tests as related to the severity of noise exposure during this period. A major difficulty in accomplishing this was the estimation of relative noise exposures of the different groups and individuals. Actually three different estimates of noise exposure were employed. Subjects were divided into most-exposed and least exposed groups on the basis of (1) the amount of noise generated by the plane which their squadron used (2) the estimation (based on responses to a

questionnaire) of a man's noise exposure during the six month period between tests, and (3) changes in his auditory threshold during the period between tests

No positive relationships were found among the three above-named criteria for severity of noise exposure. That is, a man judged to be severely exposed by one criterion would not necessarily be judged to be severely exposed by either of the other two criteria

In all, 95 of the men who were given the nonauditory tests at the beginning of the six month period were retested at the end of the period. Six of the tests, which could be administered to 10 men at a time, were given to all the subjects. The remaining 10 tests which required individual administration were given to 31 of the men

Each of the six tests that were given to all the men was analyzed according to each of the three exposure criteria and in the resulting 18 statistical comparisons\* there was only one case where the "most exposed" group performed significantly worse (at the 5 per cent level of confidence) than the "least exposed" group. The 10 tests given to the 31 men were analyzed only according to the criteria of individual exposure estimates and squadron assignment because only four subjects in this group exhibited any hearing impairment. The 20 statistical comparisons that were made with this group of tests revealed no statistically significant differences between the "most exposed" and the "least exposed" groups.

The "most-exposed" group thus showed a significant deterioration of performance on only 1 out of 38 statistical comparisons. This one significant difference obviously could have occurred by chance and it can safely be concluded that no adverse effects of noise exposure were demonstrated for this group of tests.

Although there is no statistical evidence of effects of exposure nevertheless on 26 of the 38 comparisons the "most-exposed" group actually performed worse even though only slightly worse than the "least exposed" group.

The reports to sick call by 163 men were analyzed for the total number of reports to sick call during the six month period before the initial tests and also during the six month period between tests. Changes in frequency of reports to sick call were analyzed according to the three criteria for noise exposure. The

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For the original analysis of nonauditory data the following criteria were used: (1) the test results for the two groups of subjects were compared in terms of the absolute difference in performance between the two groups. (2) Two of the subjects in the CHABA center performed better than the average of the two groups. (3) The subjects in the CHABA center performed better than the average of the two groups. (4) The subjects in the CHABA center performed better than the average of the two groups. (5) The subjects in the CHABA center performed better than the average of the two groups. (6) The subjects in the CHABA center performed better than the average of the two groups. (7) The subjects in the CHABA center performed better than the average of the two groups. (8) The subjects in the CHABA center performed better than the average of the two groups. (9) The subjects in the CHABA center performed better than the average of the two groups. 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"most-exposed" group showed a larger increase in frequency of sick call reports according to two of the three criteria but none of the differences were statistically significant.

The results of the nine factored aptitude tests were analyzed according to an estimate of noise exposure from questionnaire information. Inasmuch as performance on seven of the nine tests should be correlated with intelligence level, the intelligence level of the groups was statistically equated by use of analysis of covariance. The "most-exposed" group gave the poorest performance on eight of the nine tests but in only one case was the difference between groups statistically significant (at the 5 per cent level of confidence).

We can conclude with some confidence from the above analysis that the results in the nonauditory performances tested give no indication of a serious change for the worse as the result of greater noise exposure. Again the negative result is reassuring even though the battery of nonauditory tests was not as extensive nor was the number of subjects tested as large as we had originally planned. The result is not entirely negative however because the "most-exposed" group performed worse even though only slightly worse than the "least-exposed" group on 36 out of a total of 50 comparisons.

### Psychiatric Effects

In the psychiatric study aboard the U S S *Ticonderoga* in May of 1956 the examinations and interviews were carried out when the *Ticonderoga* had been operating in the Mediterranean for 7 1/2 months. Due to unforeseen circumstances the cruise had twice been prolonged beyond the usual six months time. During the 7 1/2 months about 1 500 catapult shots had occurred.

A group of 70 men were selected all with General Classification Test (GCT) scores above 30 who had all been present aboard the *Ticonderoga* for at least 75 per cent of the cruise. The majority of these men were flight deck personnel although not all worked in close proximity to the forward catapults and a small control group of men worked below decks with little or no exposure to noise. The men were classified with respect to noise exposure on the basis of their jobs. Thirteen had "very high" noise exposures, 18 had "high" noise exposures forward of the island structure, 13 had "moderate" noise exposures at or aft of the island and 14 had relatively "low" noise exposures.

Psychiatric rating scores were obtained for each of these men by a rather elaborate method that cannot be described in detail in this article but which aims to divide the men into a more adjusted group and a less adjusted group. The mean scores of the four exposure groups differed but little but when a cutting score was employed there seemed to be a significant

difference between the groups. The direction of the difference associated high noise exposure with deterioration of motivation or some increase in anxiety.

In addition to employing the standardized questionnaire and interview and the predetermined scoring system, the psychiatrists also noted the comments made by individual men and evaluated their reactions. Many of the subjects gave anecdotal reports similar to those in the BENOY Report. The most common complaints were increased irritability, tenseness, insomnia, and occasionally fear because of inability to communicate with other men in the presence of noise. With the exception of the difficulty of communication, however, most of the men stated that they did not believe that their trouble was due to the noise. They felt much more strongly that their trouble was due to the general dangers of the job and to further concern about a delay in their return to the United States that had been occasioned by a change in the schedule of operations of the ship.

The relative danger associated with the various jobs, therefore, was assessed. It appeared that there was indeed a greater degree of risk for the men in the very high noise exposure and the high noise exposure groups as compared with the low exposure group. The relation between the psychiatric rating scores and the probable danger associated with the job seemed to be at least as high as, and perhaps higher than, the relation between rating scores and noise exposure. This conclusion, reached by the psychiatrists from their own observations, was borne out by the statements made by the subjects themselves. Among the men working in the most dangerous jobs (involving also very high noise exposures) 92.3 per cent expressed anxiety about their jobs, while among the men working on the safest jobs just below the flight deck only 21.4 per cent expressed any anxiety about their jobs. Very few men, however, even among the high noise exposure group, expressed the opinion that the jet noise was disturbing to them.

The over all subjective impression developed in May 1956 by the two psychiatrists aboard the U S S *Trconderoga* was that the anxiety level among the men working on the flight deck was considerably greater than what they had encountered among a similar group of men interviewed aboard the same ship in the previous September about eight months earlier. Unfortunately the overlap between the earlier group studied and the final group was too small and the differences and the methods of interview employed were too large to allow any significant comparison of scores for the same individuals before and after the 7 1/2 month cruise.

It is the over all opinion of the psychiatrists that the basic reasons for the increased anxiety revealed in the psychiatric

interviews lay in the greater awareness of the inherent dangers of the jobs and in the fact that the ship was overdue for return to the States. The awareness of danger had undoubtedly been heightened by several fatal accidents that had occurred on the flight deck during the cruise. Furthermore whatever the neuro-psychiatric effects of high noise exposure may be they are subtle and difficult to extract. The present series of carefully planned and carefully conducted interviews did not reveal any easy or obvious correlations with noise exposure nor do they give any cause for alarm.

The general conclusion from our auditory, nonauditory and psychiatric observations is therefore that no one of the many functions examined in this series of nonauditory tests stands out clearly as being adversely affected by noise exposure according to any one of the three admittedly imperfect criteria used for estimating the severity of the noise exposure. There is however a definitely suggestive trend in the direction of a slight over all decrement of performance associated with the most severe noise exposures. Noise levels as of March 1957 did not constitute a serious threat for exposed personnel in terms of large changes in performances on our test battery. Because of the suggested trend toward a slight general decrement however we must view with some concern the future effects of higher noise levels and longer periods of exposure. The negative conclusions apply only to a period of six months exposure to noise sources as powerful as the F4D.

### FINAL EVALUATION

The over all result of the ANEHIN survey is definitely reassuring. Some initial auditory impairment was found among naval personnel as in the previous survey but it could not be proved that six months operational exposure to jet engine noise even with afterburners increased the auditory impairment. None of the nonauditory tests showed any really clear correlation between worse performance and greater exposure to jet engine noise. There was a slight increase in the number of sick calls and a trend toward a very general nonspecific lowering of test performance but these were merely trends. An increase in anxiety and tension was found among flight deck personnel near the end of a 7 1/2 month Mediterranean cruise but the anxiety and tensions were probably caused by hazards and stresses other than jet engine noise.

Why after the solemn warnings of the BENOX and CHABA reports was so little evidence of any cumulative injurious effects of exposure to the high intensity noise of jet engines found?

There are three definite and one rather vague answers to this question. (1) The increase in the noise produced by operational

aircraft in the fleet did not occur as soon as appeared likely when the BENOX and CHABA reports were written. One particularly noisy type of airplane never became operational and another was slow in reaching full employment. (2) The introduction of more powerful catapults had greatly reduced the use of the afterburner at take off. This has reduced the anticipated noise exposure on the carrier deck by several decibels. (3) The really severe noise exposures on the flight deck were, and still are, very, very brief.

It is for these three reasons that the ANEHIN Project found itself in the field in good time, ahead of the great anticipated increase in noise exposures on shipboard. For these reasons ANEHIN could properly transfer its activities ashore to the U S Naval Air Station, Cecil Field, Fla., where the maintenance men who service jet planes with afterburners actually incur much more severe and prolonged noise exposures than do the carrier flight deck personnel.

Even among the shore based maintenance men, the results are almost, although not quite, negative. This is sheer good fortune. The vague conclusion is that Nature's margin of safety proves to be a little wider than the authors of the BENOX report feared it might be. For the present, then, reasonable caution, observance of criteria for noise exposure, use of personal protective equipment, and the institution of appropriate monitoring procedures should suffice. How wide the present margin of safety may be we do not know but for the present we believe that further field studies of cumulative aftereffects are not needed except as part of a sampling, spot check type of monitoring. If the limits of tolerance for high intensity noise exposure are to be sought the job can be done much more cheaply and effectively under controlled conditions, as in a laboratory than as a field study.

Our final words are again a reassurance as to the present situation followed by a warning against overconfidence and complacency in regard to the future. We still have not encountered the noise stresses foreseen in the first CHABA Report.

### DISCUSSION

Doctors Nello Pace, R. C. Davis, Lyle Jones, David McK. Rioch and William Burns briefly discussed the report.

Doctor Pace remarked that relatively simple tests of adrenal cortical function based on blood and urine samples might detect underlying

Dr. P. C. Davis, Department of Physiology, University of California, Berkeley, California. Dr. R. C. Davis, Department of Psychology, University of North Carolina. Dr. Lyle Jones, Department of Psychology, University of North Carolina. Dr. David McK. Rioch, Director, Naval Air Station, Cecil Field, Florida. Army Medical School, Grady School of Medicine, U.S. Army Medical Center, Washington, D.C. and Dr. William Burns, Department of Psychiatry, University of London, England.

physiologic changes even though the person appears to be unaffected in terms of his ability to perform under stress. Doctor R. C. Da is noted that the autonomic nervous system may participate in the adjustment of the body to stress and the maintenance of performance. Doctor Jones commented that the statistical technique of analysis of covariance would partial out undesired variables especially those associated with the unreliability of a given physiologic or psychologic measure. He suggested that the use of this technique in recalculating some of the statistical data would result in much more meaningful and useful data. Doctor Rioch added that field studies often have as their major result the identification of the relevant factors in the problem and the observations that need to be made. In addition new apparatus is frequently developed that has applications beyond the situation for which it was created. The ANEHIN noise cumulator is a major contribution to the study of noise exposure in general.

Doctor Burns briefly reviewed the British Navy's research on hearing conservation in high intensity noise. The Royal Navy is placing great stress on educating service personnel on the necessity of protecting their hearing in the presence of high intensity noise. Otherwise the British work is of the same general character as the American effort with much the same conclusions. The American V-51R ear plugs are now being superseded on the carrier flight deck by the British Mk. I helmet equipped with an ear muff that incorporates a leather sealing ring as well as an acoustic valve. Other improved models of the muff are now being introduced.

#### SUMMARY

Carrier flight deck personnel on board the U. S. S. *Forrestal* and the U. S. S. *Ticonderoga* and shore based jet aircraft personnel at the U. S. Naval Air Station Cecil Field, Fla. were tested by pure tone audiometry, psychologic and psychomotor performance tests, group paper and pencil tests, psychiatric interviews and analysis of sick bay calls. The results were related to the estimated relative noise exposures of the various exposed and control groups tested.

The audiometry was conducted in a specially designed and constructed trailer laboratory by means of a group audiometer that was developed as part of the project. This semiautomatic instrument is suitable for monitoring audiometry elsewhere.

A method for the measurement of the total noise exposure of individuals during actual military operations or maintenance tasks was developed. This method relies upon a special device, the noise cumulator, which was designed, constructed and a prototype tested on board a carrier. The complete device was not, however, available until after the three field studies. This instrument is suitable for monitoring the noise exposures to be expected from future aircraft.

The battery of psychologic and psychomotor tests was composed of simple well tried tests of known significance that sampled a wide variety of sensory motor, intellectual and emotional functions

No clear, positive effects either auditory or nonsensory of exposure to noise were shown by any of our tests. Certain small positive effects were found by the audiometric and the psychiatric studies, but these are attributed to causes other than jet engine noise. A suggestive trend toward a slight general decrement in performance did appear in the psychologic tests of jet plane maintenance personnel

### CONCLUSIONS

As of March 1957, there was no reasonable cause for immediate alarm concerning cumulative aftereffects of jet engine noise exposures of naval personnel

It is unsafe to extrapolate from present noise exposures to the more severe exposures that must be anticipated in the future. The extent of the present margin of safety is not known, and continued vigilance is required

In the opinion of the ANEHIN group, at least two other undesired effects of high intensity noise were as of 1957 more serious threats to military operations than were its cumulative aftereffects. They were (1) interference with communications and (2) decrement in performance of personnel during actual exposure to high intensity noise

### RECOMMENDATIONS

Further field studies of this sort are not necessary until there is a considerable increase in operational noise exposures. Meanwhile, monitoring of noise exposures with the equipment developed by ANEHIN should be instituted to detect such changes

Monitoring audiometry and also monitoring by selected psychologic and psychomotor tests should be instituted for the protection of personnel who suffer the most severe noise exposures

Valid criteria of hazardous noise exposures should be established by carefully controlled experiments with human volunteers using careful measurements of noise exposure and the tests of the ANEHIN battery. In such experiments the decrement of performance during actual exposure to noise also should be measured

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 A. M. A. Arch Ot laryng 58 62-80 July 1953  
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### SPINNING IN A SPACESHIP

From ob rvation of the V 2 and Vik ng it appears th t these rockets spin fairly rapidly and unpredictably on their upward flight and simple an logy shows what the effect of this might be on the hum n body If you spin round and round while standing in the one position and then stop what happens? Everything else in the room appears to spin and you probably feel giddy If you now try to pick someth ng off the floor o table you experience great d fficulty in doing so This is wh t would h ppen in the rockets of today only to a greater d gree If the spinning occurs at right-angles to this that is if the crew were se ted in the spaceship then spinning would be round an axis fore and aft through the body at the lower end of the chest In this situat on con sciousness s lost fairly quickly and death might even occur Although spinning is obviously a serious hazard it is one wh ch can be avoided by design and in the future rockets will require to be stabilized

—M KENNEDY BROWNE B Sc M B CH B  
 in Sp fl ght  
 p 142 July 1957



## Clinicopathologic Conference

Tripler U S Army Hospital APO 438 San Francisco Calif

### DYSPNEA AND DYSPHAGIA IN INFANCY

**Summary of Clinical History** A two-month old Caucasian Oriental male infant was admitted to this hospital from the Pediatric Clinic on 17 July 1954. He previously had been hospitalized on 20 May, when 11 days old, for severe diarrhea. At that time his weight was 4 pounds 8 ounces, a decrease from his birth weight of 6 pounds 3 ounces. At the time of his discharge on 4 June, he weighed 6 pounds. He was seen regularly in the Pediatric Clinic. His mother stated that he had been doing fairly well at home but within the past two weeks she noted a decreased fluid intake from approximately 30 to 35 ounces per day to around 20 to 22 ounces per day. There was moderate dyspnea associated with feeding. He was last seen in the Well Baby Clinic one week prior to admission to this hospital, when his weight was 8 pounds 8 ounces. The mother said that during the three or four days immediately prior to admission his fluid intake had further decreased to the point where he was taking from 1 to 3 ounces per feeding. When seen in the Pediatric Clinic the morning of admission he was in poor physical condition. He weighed 8 pounds.

**Physical Examination** On admission the infant's temperature was 100.4°F. Physical examination revealed a moderately dyspneic, small male infant who appeared "somewhat grayish and pallid." There was no evidence of dehydration. He seemed fairly alert and in good contact with his environment. The only significant physical findings recorded at the time of admission were scattered moist rales over the left apex anteriorly and

At the time of this conference Major John F. B. Hilder, MC USA, was Commanding General of the Pathology Service. Colonel Harold E. Sherry, MC USA, Chief.



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—M KENNEDY BROWNE B S M B CH B  
 in Sp fl ght  
 p 142 July 1957

of the child's poor condition, endoscopic examination was not advisable at that time. The infant was treated conservatively for the next three days, but the apparent respiratory obstruction at about the level of the larynx continued. The nurses noted that the child took his feedings best when lying on his abdomen with his head turned to one side or the other. Feedings every three hours were instituted on 26 July. The baby began to eat more avidly and to take larger amounts, averaging approximately 150 ml at each feeding.

On the morning of 27 July when the child appeared no better he was taken to the x-ray department where Lipiodol (brand of iodized poppy seed oil) studies of the esophagus were done. Injection of the contrast medium was made through a No. 6 French catheter, placed with considerable difficulty into the upper portion of the esophagus. The report was as stated above. Later that same afternoon it was decided to attempt direct laryngoscopy. At approximately 1530 hours, the child was taken to the Ear, Nose, and Throat Clinic. The laryngoscope was introduced and when it reached the base of the tongue respirations ceased. The infant was returned to the ward and artificial respiration, continuous tracheal aspiration, administration of oxygen by mask, and intracardiac injection of caffeine sodium benzoate were all employed without benefit. The cardiac action ceased at approximately 1605 hours.

### DISCUSSION

Docto Buton: This is the story of a two-month old infant who was first hospitalized at 11 days of age because of severe diarrhea of unknown cause. We are told that he lost 27 per cent of his body weight or what would amount to approximately 40 pounds for an average sized adult because of this illness. In spite of his severe disease he was doing well enough to be discharged after two weeks. He was thought to be fairly well at home for two to three weeks and then it was noted he was feeding poorly and having moderate dyspnea with each feeding. The latter symptoms increased in severity over a two-week period so that on the second admission he was obviously in poor condition, gray and pallid, with moist rales scattered over the left upper lung field. His temperature was only slightly increased on admission and his entire 10-day hospital course was characterized by the lack of fever. His white blood cell count was moderately increased to 16,700 and 28,000 per  $\mu$ l with only 48 per cent and 39 per cent neutrophils. The roentgenogram is reported to us as showing no infiltration at that time. We will look at it later as we should on all our patients.

However, let us pause here to consider the possible causes of the symptomatology as given. Certainly, the most common and a very common one is a respiratory infection often resulting in the young infant in obstructive emphysema in which there is a marked bronchial

reaction perhaps with areas of pneumonitis and atelectasis. We call this acute bronchiolitis; others may call it acute interstitial pneumonia and in its milder form and in older infants and children it may be called asthmatic bronchitis. These conditions are usually much more acute than described in this infant and may be so fulminating as to result in death in a few hours. Although upper respiratory infection may precede lower respiratory symptoms, such an event rarely occurs in such an insidious manner as in this infant. Rales, fine and diffuse, are almost regularly heard and roentgenograms usually show depression of the diaphragm with other evidence of emphysema which may indeed cover up any other process present in the lungs. Although this infant may have had a mild respiratory infection, we do not have the usual findings associated with this type of fatal respiratory disease.

With cyanosis and dyspnea we must mention congenital heart disease, but in the absence of murmurs, change in heart size, and lack of polycythemia we really have no clues to lead us to a serious consideration of a cardiac lesion.

A bilaterally obstructed nose may lead to marked distress in young infants. This may occur during the first hour of life if congenital or later if due to swollen mucous membranes from infection or other insults. It is not unusual for a week-old infant to be admitted to a pediatric ward in marked distress, thought to have cyanotic heart disease, and by simply opening his mouth have all the signs disappear. The observers of this infant did not believe that obstruction was present in the nose, and we can accept this to rule it out.

From the two extremes already mentioned, our attention is focused on a more middle ground around the larynx inasmuch as those observing the patient seemed to think he had a laryngeal obstruction. In this age group one naturally thinks again of congenital defect. The clinicians properly excluded a vascular anomaly constricting the trachea and esophagus by observing a contrast medium take a normal undisturbed course down the esophagus. Other congenital defects like stenosis of the larynx and trachea and the usual form of tracheo-esophageal fistula with esophageal atresia would be evident shortly after birth. We have to postulate the an acquired lesion and/or a lesion which gradually encroached more and more on the infant's airway and esophagus. Various tumors of the larynx could do this: hemangioma, adenoma, papilloma, cystoma, fibroma, lipoma, lymphangoma, chondroma, et cetera. These must be extremely rare in infants of this age, and lacking any positive evidence for their diagnosis, the more common type of tumor caused by infection must be given first consideration. The course of retropharyngeal abscess appears to be consistent in most details given us with the course of illness observed in this infant. It is distinctly a disease of infancy, most cases occurring in the first year of life, and it is almost never seen after the age of three years. Origin is usually a sequel to acute infection in the nose and throat. Infection localizes in the retropharyngeal lymph glands which overlie the second and third cervical

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1. The first part of the document is a list of names and addresses, which are arranged in a columnar format. The names are written in a cursive script, and the addresses are written in a more formal, printed style. The list is organized into three main sections, each separated by a horizontal line. The first section contains names and addresses, the second section contains names and addresses, and the third section contains names and addresses.

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5. The fifth part of the document is a list of names and addresses, which are arranged in a columnar format. The names are written in a cursive script, and the addresses are written in a more formal, printed style. The list is organized into three main sections, each separated by a horizontal line. The first section contains names and addresses, the second section contains names and addresses, and the third section contains names and addresses.

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Jackson and Jackson<sup>1</sup> in Diseases of the Nose Throat and Ear admonished the reader to exercise care in the treatment of these cases as incision of the abscess may result in flooding of the pharynx with

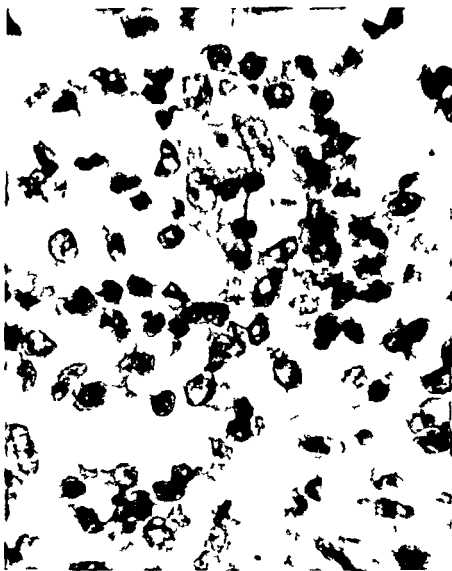


Figure 3. Photomicrograph of bacterial wall, leukocytes and inflammatory cell infiltrate (H&E stain, x285)

pus and blood causing asphyxiation. They also stated that death has occurred at the time of insertion of a mouth gag apparently as a result of acutely obstructing an already diminished air passage.

As Doctor Bruton has mentioned, retropharyngeal abscess occurs most commonly in infants and young children. Pyogenic bacteria set up an inflammation in the nose or pharynx or occasionally the ears.

The lymph nodes in the upper posterior wall of the pharynx then become infected and suppurate. These nodes generally disappear in a few years accounting for the rarity of this entity in older children.



Figure 4 Photomicrograph of abscess wall, trachea and thyroid gland. The trachea and thyroid were not involved by inflammation (Hematoxylin and eosin stain  $\times 7$ )

The chief complications of retropharyngeal abscess are extension retroesophageally into the mediastinum, rupture into the pharynx with aspiration of pus, erosion into the internal carotid artery with fatal hemorrhage and laryngeal edema. Clinically there may be dyspnea, dysphagia, cervical adenopathy, fever, sore throat, cough and convulsions.

case could then be fitted into an epidemiologic and pathogenetic pattern that has been observed all too frequently since the first recorded observation of the development of penicillin resistant Staphylococci 9 or 10 years ago

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 Ear W B S under C Ph l d lphia P 1945 p 151  
 2 W ll F L. d D Bl E R tr phary g l b pr bl m in tr m  
 Arch Ot laryng 39 344 347 Ap 1944

## ALCOHOLISM IN AUSTRALIA

Perhaps the largest and most important group of all alcoholics is made up of normal but rather immature men whose emotional development has been retarded at the man's man stage of development. Good army canteen and mess men, good shipmates, good sportings fans, good clubmen, good lodge men, good mates, good fellows, all they prefer the company and conversation of the own to that of the opposite sex—in their youth without and later with the stimulus of alcohol. They behave together much like overgrown schoolboys. They will leave the lounge for the brass rail at licensed establishments and at mixed parties congregate around the beer keg and the whisky decanter. Coeducation, increased opportunities and increased emphasis on social intercourse between the sexes, civilized mixed drinking at sidewalk cafes and ritual evening long dinners with mixed company and good conversation would all help a would increasing emphasis on the role of the woman in our society—a trend toward matriarchy and the importance placed by the troubadour on his lady as important in his life and community affairs.

—WILFRED RICHARDS

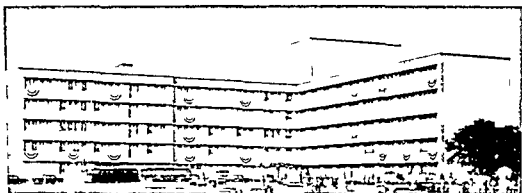
M d l J m l / A t l

p 546 Oct 12 1957

### AIR FORCE DEDICATES 250 BED HOSPITAL AT CARSWELL AFB FORT WORTH, TEXAS

A new 250 bed hospital completed at a cost of \$5 200 000 was dedicated in formal ceremonies at Carswell Air Force Base near Fort Worth Tex on 24 May The principal address was given by Major General Dan C Ogle Surgeon General of the Air Force before a crowd of more than 500 military and civilian guests of the air base

Construction of the new hospital was begun on 12 July 1955 and completed in February of this year It was informally opened for the admission of patients on 9 March The building is entirely air conditioned and is equipped with centralized oxygen and vacuum systems and an audio visual paging unit The hospital which will serve as an orthopedic center as well as treatment facility for the air base is under the command of Colonel Louis K Pohl USAF (MC)



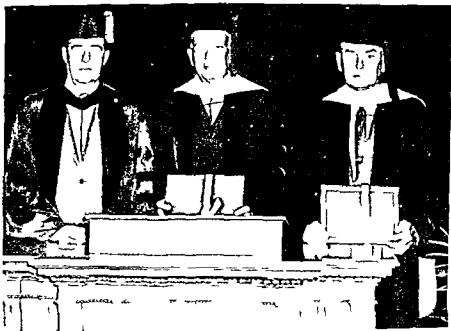
*U S Air Force Hospital Carswell Air Force Base Texas*

In addition to General Ogle the distinguished guests present for the dedication ceremonies included Dr William E Flood President Tarrant County Medical Society Dr Carl A Gibbe President Fort Worth Dental Society Mr Clay Berry President Fort Worth Chamber of Commerce Major General John P McConnell USAF Commander Second Air Force Barksdale Air Force Base Louisiana Brigadier General Nils O Ohman USAF Commander 19th Air Division Carswell Air Force Base and the following senior officers of the Air Force medical service Brigadier Generals Victor A Byrnes James C Cathroe Loyd E Griffis and M S White



## HIGH RANKING MEDICAL OFFICERS GIVEN HONORARY DOCTOR OF SCIENCE DEGREES

Major General Leonard D. Heaton MC USA Commanding General Walter Reed Army Medical Center and Rear Admiral Edward C. Kenney Assistant Chief of the Bureau of Medicine and Surgery for Personnel and Professional Operations received honorary degrees of Doctor of Science from Denison University Granville Ohio at the 117th annual commencement exercises on 9 June.



*Dr. Knapp, General Heaton and Admiral Kenney*

The degrees conferred by Doctor Albert Knapp, President of the University, were accompanied by citations which read in part to Leonard Dudley Heaton, loyal alumnus, skillful surgeon, eminent hospital administrator, faithful servant of his nation in war and peace, and to Edward Christopher Kenney, loyal alumnus, talented physician and medical researcher, eminent hospital administrator, lifelong servant of his nation in peace and war, the degrees of Doctor of Science.

General Heaton attended Denison from 1919 to 1922 prior to studying medicine at the University of Louisville. Admiral Kenney received a Bachelor of Arts degree in 1926 and subsequently was awarded a Doctor of Medicine degree from the University of Cincinnati.

## NEW COMMANDER OF NAVY LABORATORY

Captain John R Seal MC USN recently assumed command of the U S Naval Medical Research Unit No 3 in Cairo Egypt The change of command ceremonies were attended by a group of dignitaries in



*Ambassador Hare left and D Seal*

cluding United States Ambassador Raymond A Hare to the United Arab Republic and Captain Charles S Moffett USN Naval Attache Captain Seal was formerly head Communicable Disease Branch Bureau of Medicine and Surgery

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### Correction

The name of Advisory Council on Reserve Affairs to the Surgeon General of the Army was given incorrectly on page 751 of the May Journal in a story concerning the group's first 1958 meeting in Washington

## A D A PRESIDENT MEETS U S AND JAPANESE DENTAL OFFICERS DURING TRIP TO FAR EAST

Doctor William R. Alstadt, Little Rock, Ark., President of the American Dental Association, recently visited United States military installations in the Far East after attending the second Asian Dental Congress and the Asian Pacific Dental Conference in Manila, Philippine Islands.



Left to right: Col. I. Burg, Capt. L. G. D. Alstadt, Dr. S. to C. I. I. H. ka, and Colonel W. d. er.

During a six-day tour of Japan on the invitation of the Japan Dental Association, he was guest of honor at a banquet at the U. S. Army Medical Center, Camp Zama, near Yokohama, attended by a group of United States and Japanese dental officers. Among those greeting Dr. Alstadt on this occasion were: Colonel Howard N. Burgin, DC, USA, Staff Dental Surgeon, U. S. Army in Japan; Captain Victor A. LeClair, DC, USN, Commanding Officer of the U. S. Naval Dental Clinic, Yokosuka; Colonel Glynn B. Widner, USAF (MC), Chief of Dental Services, Fifth Air Force, Fuchu Air Station; Colonel Tsuneo Hosaka, Chief Dental Officer of the Japan Self-Defense Force; and Doctor Kazuo Sato, President of the Japan Dental Association.

## A MESSAGE FROM THE A M A

This month the American Medical Association's Bureau of Health Education has prepared a message on the vital subject of the fitness of American youth

A great deal of attention is being attracted by claims that American youth is soft, and compared with European youth, weak and in poor condition. The conclusions are controversial, but there hardly can be any controversy about the fact that modern living, with all of its conveniences and labor saving devices, tends to reduce the amount of physical activity performed by most people, including our young people

Where American youth formerly walked to school, we now have school buses. Practically every family has a car and very few persons walk as much as a block to do an errand. Baseball, football, basketball, hockey, and other popular sports provide active participation for a few, while millions sit in the spectator seats eating hot dogs, drinking beer or soft drinks, and exerting themselves only enough to suggest killing the umpire.

The President of the United States has called conferences on the fitness of American youth. The first was held at Annapolis in June of 1956 after being postponed from September 1955 because of the President's heart attack. The second conference was held at West Point in September of 1957. Both conferences were attended by selected citizens serving as individuals but representative of medicine, education, public officialdom, the armed services, amateur and professional athletics, the mass communication agencies, and various other groups.

The Annapolis conference recommended the creation of a Council on Youth Fitness at cabinet level, plus a Citizens Advisory Committee. The President promptly created a council consisting of the Vice President as Chairman, the Attorney General and the Secretaries of Agriculture, Defense, Interior, and Health, Education, and Welfare. The second meeting at West Point was participated in by the Council and the Advisory Committee consisting of 100 citizens appointed as individuals. Included among these were six physicians and two dentists exclusive of public health personnel. The Vice President retired as Chairman of the Council and was succeeded by the Secretary of the Interior shortly after the 1957 West Point conference.

The purpose of the Council is to stimulate public interest in the fitness of youth and to encourage and help to co-ordinate efforts toward achieving youth fitness through existing official

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and voluntary agencies rather than to create a new operating department for fitness. The Director of the Council is Shane MacCarthy J D educator author and lecturer with a dynamic personality and an abundance of personal fitness.

The place of the medical profession in the fitness program is to advise at the local and state levels those agencies which are stepping up their programs in response to the Federal stimulus. The medical profession with the co operation of educators, can be extremely valuable in keeping the fitness program on a sound scientific basis and out of the hands of fanatics cranks or political and commercial self seekers.

In the absence of any generally accepted valid tests for fitness the test for success in improving the fitness of American youth must be the practical one of living. Fitness therefore must be more than mere muscular or physical competence. It must extend into the mental emotional and social facets of living. It cannot be a fixed quantity but must be adaptable to the needs of the individual. Not every young man can adapt himself to the flying trapeze nor every girl to the ballet. For whatever object the individual may have in life he must with the aid of the best available professional advice prepare himself to be fit for that achievement.

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## Journal Seeks Civilian Associate Editor

The *U S Armed Forces Medical Journal* is seeking a civilian physician for appointment as Associate Editor under the provisions of Department of Defense Directive No 51545 5 January 1957 (and change 1 21 May 1957) subject The Armed Forces Medical Publication Agency. A Civil Service grade of up to GS 15 with a top salary of \$13,970 per year has been established for this position which officially will be that of Deputy Director of the Agency.

Physicians interested in this new position which will require full time residence in Washington D C should make a formal application prior to 1 August 1958 to the Director Armed Forces Medical Publication Agency 2300 E Street N W Washington 25 D C. Applicants must be United States citizens not over 40 years of age and graduates of approved medical schools in the United States or Canada. Other requirements include a one year accredited internship plus at least two additional years of clinical experience and a minimum of five years in medical editorial work.

# OFFICERS CERTIFIED BY SPECIALTY BOARDS

## Supplementary Listing

The Surgeons General of the military medical services have announced that the following regular Medical and Dental Corps officers have been certified by the boards indicated since the listings published in previous issues of the *Journal*

### American Board of Orthopedic Surgery

D D Goldshaw : Capt. USAF      John W Howard Comd' USA

### American Board of Urology

Prince D Beach, Lt. Col. USA

### American Board of Obstetrics and Gynecology

Cowell T Daniel Jr. Maj. USA

### American Board of Internal Medicine

Bruce F Chandler Maj. USA      John R. Gibbs Lt. Col. USA

### *Cardiovascular Diseases*

James A. Orbis Lt. Col. USA

### American Board of Ophthalmology

Thomas J Tread Capt. USAF

### American Board of Surgery

George S. Benjamin Jr. Maj. USAF      Martin A Plotenberger Jr. Lt. Col. USA  
Guth B Dittger Maj. USAF

### American Board of Oral Surgery

Kenneth W High Lt. Col. USA      Rodrick L. Little Lt. Col. USA

## OFFICIAL DECORATIONS

The following awards were recently announced by the Department of the Air Force

### Legion of Merit

Dodd E Hudock Col. USAF (DC)      Benjamin A Strickland Jr. Col. USAF (MC)

### Air Force Commendation Medal

Howard B. Niso Col. USAF (MSC)

## POSTGRADUATE PROFESSIONAL COURSES OFFERED MEDICAL SERVICE OFFICERS

The following Postgraduate Professional Short Courses for Army Medical Service Officers are announced for the second quarter Fiscal Year 1959. Personnel interested and eligible to attend should apply through channels to The Surgeon General, Department of the Army, Washington 25 D C. Attention MEDCOM CG.

Prosthodontics—Letterman Army Hospital 6-10 October 1958. Walter Reed Army Medical Center 8-12 December 1958.

The purpose of this course is to provide a comprehensive review of the principles and practice of prosthodontics. It is designed for dental officers who are assigned or may be assigned to a dental prosthetic service. It encompasses an evaluation of the prosthodontic problems in the armed services and the utilization of the Central Dental Laboratory as an adjunct service to clinical practice. Examinations, diagnosis, treatment planning, and prognosis for complete and partial dentures are stressed. Special attention will be given to preparation of the mouth for partial dentures to include occlusal, incisal, and cingulum rest preparations, surveying, and designing. Considerable attention is directed to immediate dentures, impressions, master casts, and jaw relationship record for complete and partial dentures. Selection, arrangement, and articulation of artificial teeth with regard to esthetics and phonetics are presented. Table clinics and patient demonstrations will be included, utilizing color television as a teaching aid.

Anesthesiology—Army National College of Podiatry—Brooke Army Medical Center 6-11 October 1958.

This course is designed to provide opportunity for nurses and therapists to appraise and plan for the practice of anesthesia applicable in Army situations. It will cover but not be limited to: new drugs and techniques, probable role of the nurse anesthetist in a catastrophe, standard supplies and equipment, problems confronted by the nurse anesthetist in Class I installations, psychological aspects of anesthesia in relation to the patient and to the nurse anesthetist, the relationship of the nurse anesthetist to total patient care, in-service education and professional and personal problems.

Forensic Pathology—Armed Forces Institute of Pathology 6-11 October 1958.

This course is designed to provide training in medicolegal medicine to hospital pathologists and officers in charge of laboratories both in military and civilian practices. An attempt is made to orient the pathologist and assist him in coping with problems that daily arise where legal factors may be involved. The material is presented by selected specialists in the field of legal medicine. In presenting

the program lectures panel discussions slide reviews demonstrations and closed circuit TV are used Some of the subjects covered are military law sudden death obscure homicide medicolegal autopsy gunshot wounds traumatic death identification burned bodies asphyxial deaths criminal abortion cutting and stabbing serology in legal medicine death by poison doctor in court trace evidence and trauma in tumors and infections Most of the material discussed is not found in medical textbooks and periodicals and therefore fills a gap in much needed information

**Biostatistics—Walter Reed Army Medical Center 10-24 October 1958**

This course is a portion of the nine month Military Medicine and Allied Sciences Course which is a sufficiently discrete section to be offered separately Familiarity with the basic nomenclature and principles of statistics as well as mathematics is a prerequisite A review textbook reading assignment will be sent to prospective students in advance to help achieve this preparation and the first two days of the course relates statistical methodology to the design of laboratory experiment and the evaluation of data This course is intended particularly for those engaged in research and first priority will be given to students in this category

**Examination for Radioactive Contamination of Food—Walter Reed Army Medical Center 13 October 5 December 1958**

The course has been designed to train military veterinary laboratory officers in methods of detecting and measuring radioactive contamination of foods and in the basic technics for the use of radioactive isotopes as diagnostic and research tools The scope of the training will cover technics used in assaying different food products for radio contamination and to a limited extent identification of the activity Sufficient background material will be presented in the fields of mathematics nuclear physics tracer chemistry radiation biology radiologic safety and instrumentation to enable the laboratory officer to employ assay technics and to intelligently evaluate specific problems that may arise in the field Attendance will be limited to laboratory officers who have completed the radiologic health course at the Institute of Nuclear Studies Oak Ridge Tenn

**Present Concepts in Internal Medicine—Letterman Army Hospital 27-31 October 1958**

This course will encompass the most recent developments in the field of cardiovascular diseases general medicine hematology gastroenterology diseases of the chest and endocrine disorders

**Application of Histochemistry to Pathology—Armed Forces Institute of Pathology 27-31 October 1958**

The course consists of a basic and comprehensive survey of chemical and physical methods that can be used by the pathologist for the study of sections of tissue under the microscope The subjects



include a review of the theoretical basis of histochemical and classical staining methods the practical histochemistry of groups of chemical compounds such as carbohydrates lipids pigments and enzymes and the histochemistry of particular organs such as the kidney and pituitary gland The material will be presented by seminars laboratory demonstrations and the study of microscopic slides

I n s t i t u t e A m y M d i l S p l i t C p O f f i —Walter Reed Army Medical Center 28 November 1958

This institute is planned as a workshop and will provide an opportunity for AMSC officers to discuss not only trends and developments within their specific professional specialties but also current Army policies regulations and procedures pertaining to the Corps The scope of the institute will include common sessions directed toward increasing awareness and understanding of the human relations factors in organizational effectiveness leadership group participation and communication

N l g l t h M d i l M g m t F M C l i —Walter Reed Army Medical Center 38 November 1958

This course is designed to acquaint nurses with the medical aspects and problems of nuclear warfare to familiarize them with the multidisciplinary approach to the situation and to provide them with an opportunity to explore together ways in which the Army Nurse Corps may prepare for the expanded role expected of nursing personnel in national defense Present concepts and principles of the medical management of mass casualties will be highlighted

J m C K i m b g h U l g l l S m l —Brooke Army Medical Center 35 November 1958

This course will include recent advances in clinical urology and the basic sciences as applied to the field of urology The presentation of subjects of general urologic interest based on original work or clinical material will be encouraged About 10 per cent of the course time will be allocated to the presentation of interesting or unusual case reports and x-ray films

M g m t F M C l i —Brooke Army Medical Center 15 December 1958

The purpose of the course is to indoctrinate officers of the military medical services in current concepts on the management of casualties resulting from the employment of nuclear weapons The course provides up-to-date information of an undissimulated nature on the medical aspects of nuclear warfare to reduce this information to readily accessible

and useful data in the solution of problems that might arise and to stimulate thinking on ways of coping with the problem of casualties that might result from nuclear weapons employment

**Institute for Executive Officers—Walter Reed Army Medical Center 16 December 1958**

This institute will provide appropriate training for officers currently assigned or expected to be assigned as executive officers in Army hospitals or in the office of Army Command Surgeons. Training will comprise such fields as hospital organization and administration programming and budgeting the Hospital Command Management System preparation of operating plans and in service education programs conference technic review analysis and evaluation of operating results management functions preparation of hospital directives and reports integrated data processing staff and public relationships discussion of frequently recurring problems policies regarding care of military dependents organization and functions of OTSG and Army Surgeon offices

**Pathology of Diseases of Laboratory Animals—Armed Forces Institute of Pathology 8-12 December 1958**

The course is designed to provide training for professional officers who are responsible for the recognition and interpretation of lesions in experimental animals or have charge of procurement and maintenance of animal colonies. It particularly is intended to help them interpret natural diseases which may negate experimental results or influence the supply of laboratory animals or their suitability for experimental use. It is aimed especially at the needs of various Army Navy and Air Force laboratories most of which have veterinary officers in charge of their colonies. Pathology will be the theme of the course but this facet will be used as a point of departure for discussion of etiology diagnosis and control of the diseases under consideration. Special attention will be paid to those conditions that may affect the suitability of laboratory animals or may alter or interfere with experimental results. The course will be of value only to those individuals qualified to understand disease processes and to absorb information in the field of pathology. Veterinary pathologists should find the course of particular benefit but pathologists veterinarians and others with similar professional backgrounds also will find the course of value.

**Pediatric Nursing—Walter Reed Army Medical Center 8-13 December 1958**

This course is designed to provide an opportunity for nurses to appraise and plan for needs of children for comprehensive nursing care applicable in Army situations. Emphasis will be placed on recent developments and trends in clinical aspects of the pediatric care of children suffering from medical and/or surgical disease conditions.

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## Reviews of Recent Books

**CHEMISTRY OF LIPIDES AS RELATED TO ATHEROSCLEROSIS** A Symposium compiled and edited by *Irvin H. Page M.D.* 342 pages illustrated. Charles C Thomas Publisher Springfield Ill 1958. Price \$8.50

This volume is a publication of a symposium attended by investigators of the metabolism and chemistry of lipids

Fascinating speculations and interesting problems but few solutions are presented. The nature of this volume is best shown by listing phrases which abound in it. Only a beginning has been made fragmentary knowledge unsolved problem challenging and complex problem has not been explained these data cloud the validity. It is apparent that the reader will harvest a crop of question marks not answers.

A printed volume intended to be helpful should represent distilled logically presented observations and interpretations conclusions and recommendations for definitive action. It is questionable whether a report of any symposium is worth putting into print because presentations and discussions are usually diffuse and speculative experts prefer to discuss challenging problems controversial aspects and theories rather than widely accepted conclusions. This book is no exception. Therefore although the dust jacket states the volume is intended to appeal particularly to "those in all types of food industry physicians interested in blood vessel disease and epidemiologists" it is unlikely to be of value to such persons or indeed to any practicing physician regardless of specialty. In brief this book is a glorified type of minutes of a meeting.

—ROBERT J. HOAGLAND Col. MC, USA

**LABORATORY MEDICINE—HEMATOLOGY** by *John B. Miale M.D.* 35 pages 192 illustrations and 9 plates including 5 in color. The C.V. Mosby Company St. Louis Mo 1958. Price \$13.75

This is taken from the Foreword by *W. A. D. Anderson*. Laboratory medicine has lagged behind its true role in medical practice in both the general education of physicians and in the evaluation of clinical pathology as a specialty of medical practice. From the Preface by Doctor Miale the author "This book on Hematology and two others in preparation on Chemical Pathology and Microbiology emphasize the correlation between laboratory and clinical data. It ranges from basic mechanisms to the interpretation of laboratory data in diagnosis and therapy. Only tests which are ordered with discrimination performed with skill and interpreted with understanding yield significant data."

The book is in general a rather sophisticated presentation of the physiology and physiopathology of the formation function and destruction of blood elements. It is a commendable attempt to provide a coherent and contemporary background for the practice and inter

pretation of hematologic laboratory procedures. It is up to date as of 1955 with a few references in some sections as late as 1956.

It is not a book without flaws. Overall it gives the impression of a work of scholarship rather than experience and the author's attitude seems sometimes to be uncritical. The text has many minute errors of fact which do not seriously detract from its worth. Some of the illustrations are not good. The color plates of the blood and marrow cells are the worst this reviewer has seen. Diagrams such as Fig. 87. The major factors concerned in erythropoiesis and Fig. 99. Catabolic pathways of hemoglobin are overly generalized and inaccurate. Fig. 20. Aspiration of sternal marrow demonstrates the needle lodged in the sternum rising out of a great bushiness of unshaved chest hair in disregard of the most elementary preparation for a surgical procedure. The photomicrographs of the red cells generally lack contrast or definition or both.

These are minor disparagements of a valuable book. It is indeed the best of its kind. —WILLIAM H. CROSBY, Lt. Col. MC, USA.

**FAT CONSUMPTION AND CORONARY DISEASE: THE EVOLUTIONARY ANSWER TO THIS PROBLEM** (A book of 40 pages) by T. L. CLARK, M. R. C. P. (Lond.)  
Foreword by Percy St. Clark, C. M. G., M. A., M. D., F. R. C. P., F. S. S.  
40 pages. Philadelphia: Library of New York, 1958. Price \$2.50.

This small 40-page monograph outlines a new concept correlating coronary disease with fat consumption. The author applies the Darwinian theory of evolution and the natural law of adaptation to explain an instinct of appetite. He proposes the principle that an organism may rely on this instinct to tell it what it should eat but only as long as the instinct is being exercised on natural substances that are on substances occurring in the natural environment of the organism.

In civilized countries the instinct of the appetite fails because of the many unnatural substances especially concentrated fats as butter, chocolate and shortening and concentrated sugars. Combinations of these unnatural substances he calls arbitrary food mixtures and the consumption of these unnatural fats is offered as the cause of coronary atherosclerosis. The author also gives a brief discussion on the proper selection of diet to prevent this disease.

—DOSS O. LYNCH, Lt. MC, USA.

**FUNDAMENTALS OF NEUROLOGY** by Emory G. Gardner, M. D., 3rd edition, 388 pages, illustrated, published by W. B. Saunders Company, Philadelphia, 1958. Price \$4.75.

Textbooks may be provocative or noncontroversial. Often a little of both appears. Gardner's *Fundamentals of Neurology* is such a book. This neatly bound clearly printed 388 page volume in its third edition strives valiantly to introduce the author's conception of neurologic principles to an audience of undergraduates including nurses, physiotherapists, occupational therapists and medical students.

Physiology and anatomy of the nervous system are discussed with brief excursions into pathology and clinical neurology. Homely analogies are freely used on occasion effectively. Most of the photographs are superb and many line drawings help to clarify the text. Each chapter is briefly summarized and followed by short biographies of investigators mentioned therein. Chapter references are few but well chosen and nicely described by the author. A glossary and an adequate index complete the book.

An astonishingly detailed chapter on microscopic anatomy of the nervous system makes the gross anatomy presentations appear glaringly scanty. An excellent chapter on excitation and conduction contrasts sharply with the confusing discussion of the forebrain. Throughout the book such inequalities occur. At times too elementary, the book is often beyond the author's avowed audience. Few nurses could read this book and gain more than a blurred image of the nervous system. For a medical student it is neither an anatomy or physiology text. This reviewer indeed found the good chapters provocative but the vague ones narcotizing. The book is only recommended for serious students having access to well stocked medical libraries.

—HENRY W. HOGAN Maj MC, USA

THE PRACTICE OF INFECTIOUS DISEASE by Louis Weinstein Ph D  
M D 501 pages Landsberger Medical Books Inc New York N Y  
Distributed by the Blakiston Division of the McGraw-Hill Book Co  
New York N Y 1958 Price \$8.50

The preface of this book contains the inference that the practice of infectious disease is being so changed by the use of chemotherapy that past concepts need to be modified. Advertised as a "handbook for general practitioners" it is a volume of short essays. No attempt at easy reference or special cross indexing has been made which has become the generally accepted form of a handbook for busy practitioners. The first three chapters are short essays on the principles of the treatment of infections which set the tone of the book as the new approach to infectious disease. Other chapters are a discussion of infectious disease by anatomic region and organ systems in the form of short essays many too brief to be much more than dictionary descriptions and the final one on fever of obscure origin dwindles off into an outline and ends in platitudes. The book is easy to read but does not fulfill in a convincing form the thesis stated in the preface. It certainly is not a handbook for ready reference for the general practitioner. The book is poorly bound and contains frequent typographic and occasional editorial errors: *e* on page 66 line 4 to kill *Anophelene* species of mosquitos.

—WILLIAM D. PRESTON Col USAF (MC)

DRUGS OF CHOICE (1958-1959) edited by Walter Modell M D 931 pages illustrated The C. V. Mosby Company St. Louis Mo 1958 Price \$12.75

This is a remarkably good book. The editor has assembled the written thoughts of 37 clinical specialists concerning drugs used in their

fields. Each chapter is laconic, readable, and full of information which is personalized and at times superfluous.

It will serve a useful purpose in every hospital library where the house staff can review the clinical uses of drugs in a particular field in a matter of minutes. The book contains too little pharmacology to be useful to medical or graduate students.

In my opinion there is only one drawback to the book. There is no true need for it. The scope of this book is at present adequately handled by the *New and Nonofficial Drugs*. Personally I cannot abide a book as expensive as this which announces that it will be obsolete within 18 months following the purchase of the book.

—EDWARD J. HUYCKE, Capt. MC USA

HEART DISEASE IN INFANCY AND CHILDHOOD by J. H. D. K. M. D.  
R. H. D. R. W. M. B. F. R. C. P. d. P. t. V. I. d. M. D. 877 p. \$  
Illustrated. Th. M. M. L. C. M. p. y. N. W. Y. k. N. Y. 1958. P. \$22.50

The authors of this comprehensive text on the most recent knowledge of heart disease in children have drawn freely from the world literature and their own 20 years of experience in the cardiac section of the Hospital for Sick Children at Toronto, Ontario. In one five-year period they studied more than two thousand patients with heart disease, the majority having congenital malformations.

The first chapters include an excellent discussion of physical diagnostic methods and describe the embryology of congenital and acquired cardiac defects. Subsequent chapters cover the incidence, pathology, hemodynamic, electrocardiography, cardiac catheterization, angiography, diagnosis, prognosis, and treatment of congenital cardiac disease.

The last section of the book discusses cardiovascular manifestation and associated findings in acquired heart disease. Included among these are rheumatic fever, collagen disorders, arrhythmias, myocarditis, pulmonary heart disease, glycogen storage disease, and the effects of thyroid, electrolytes, anemia, and renal and neuromuscular disorders on the heart. There are also good discussions of the cardiac disorders in mongolism, Marfan's syndrome, cardiac tumors, gargoylism, and congestive failure.

Three appendices contain a concise discussion of pre- and postoperative care, a table of pertinent drugs and dosage, and a fold-out chart summarizing the clinical features and treatment of congenital heart disease. One significant error was detected on page 852, the digitalizing dose of digoxin given as 0.3 mg per lb instead of 0.03 mg per lb.

This book is clearly written well organized and adequately illustrated. Each chapter is supplemented by an up-to-date bibliography. It should be of great value to every general practitioner, pediatrician, internist, cardiologist, and medical student.

—ANDREW M. MARGILFTH, Comdr. MC USN

**BONE DISEASES in Medical Practice** by I. Snapper M.D. 229 pages with 24-page section of 48 plates. Crane & Stratton Inc. New York N.Y. 1957 Price \$15

This authoritative text is divided into 31 chapters. The leading chapter deals with the physiology of bone and the second short one on the radiologic examination. The subsequent chapters with the exception of the last deal with the difficult diseases in which bone and other tissues are involved. Each disease is discussed in adequate chronological sequence including complications. The last chapter deals with differential diagnosis of bone disease. It is a comprehensive and informative 22 pages. The index is followed by 48 pages of radiologic prints produced with very good fidelity. Each chapter is followed by appropriate references. A number of chapters and tables are included. Although the index may be considered as rather brief by some readers in general it appears to be adequate.

This should be a valuable reference volume to the internist, pediatrician, endocrinologist and those engaged in isotope techniques.

—FRANCIS W. PRUITT Col MC USA

**PRACTICAL CLINICAL CHEMISTRY. A Guide for Technicians** by Alma Hille Ph.D. 265 pages. Charles C Thomas Publisher Springfield Ill. 1957 Price \$6.50

This second edition of this monograph presents a glossary of 26 biochemical procedures in clinical diagnostic techniques that covers the usual routine requests made by physicians. Three chapters are devoted to general laboratory procedures, standardizations of reference solutions, and photometry. As in the previous edition, each determination is presented initially in detail and in an outline operational form which may be detached from the book if desired. This is advantageous as these can be removed, placed in transparent covers and used by the technicians performing the procedures. The procedures presented are well established and accepted through common usage; several have been slightly modified in the interest of simplicity and economy of time without sacrifice of accuracy. This book is of value to those working in or directing an average diagnostic laboratory. The extent of revision in this edition, however, would not appear to justify replacing a copy of the first edition. —WILLIAM H. LEE, Lt Col USAF (MC)

**TUMORS OF THE SOFT SOMATIC TISSUES. A Clinical Treatise** by George T. Pack M.D., LL.D., F.A.C.S. and Irving M. Ariel M.D., F.A.C.S. 820 pages, 652 illustrations. Paul B. Hoeber Inc. Medical Book Department of Harper & Brothers New York N.Y. 1958 Price \$30

This volume is a very comprehensive reference on tumors of the soft tissues. It is written by Doctors Pack and Ariel and a group of 15 collaborators and is based upon 25 years of work and a total of 717 cases of these tumors. Technically the book is well prepared and bound. The type is legible and errors are at a minimum.

The soft somatic tissues are defined by the authors as consisting of connective tissue, fat, muscle, fascia, synovia, blood, and lymph.



vessels and nerve tissue. Each chapter is profusely illustrated with drawings, charts and photographs. There is a bibliography at the end of each chapter and an index at the end of the book.

This book is well written and well organized as it must be to cover such a wide field. The recommended therapies are based primarily on the personal experience of the author and alternative methods are described and appraised. As a matter of interest, the over-all 5 year survival reported is 39 per cent.

Altogether this is an excellent reference that fills a definite gap in the libraries of those interested in the treatment of tumors.

—PHILIP D. CRONMILLER, Capt. MC, USN

**THERAPEUTIC HEAT** Volume II of Physical Medicine Library edited by S. de L. Holt, M.D. 466 pages. Illustrated. Cloth. \$12. New York: C. 1958. P.

*Therapeutic Heat* is the second volume of the series to be known as the Physical Medicine Library and is a welcome addition to the growing list of textbooks on physical medicine and rehabilitation.

This volume offers a comprehensive coverage of the subject of heat, presenting all aspects of its clinical uses. The great variety of therapeutic apparatus and methods for applying heat are described. The physiologic effects, techniques of application, dosage and indications and contraindications for the modalities in clinical use are clearly presented and should be of value to clinicians in general. In addition, there are individual chapters devoted to the use of heat in rheumatic diseases, orthopedics, peripheral vascular diseases, neuromuscular disorders, pelvic diseases and diseases of the eye.

For the physiatrist and student of physical medicine who needs to extend his knowledge of the technical and biophysical principles involved, it is gratifying to find several chapters devoted to detailed presentations of the physics of heat, the biophysics of diathermy, microwave, ultrasound and thermometry.

The book is a valuable contribution and should be of real value to all physicians practicing and teaching in the field of physical medicine and rehabilitation. —ANIELLO F. MASTELLONE, Lt. Col. MC, USA

**THE TREATMENT OF FRACTURES** by L. N. B. Holt, M.D. Volume III. Translated from the Thirtieth German Edition by Alf. de W. Holt, M.D. Oxford: M.D. 2307 pages. 1699 illustrations. Grun. and Str. 1. New York: N.Y. 1958. Pn. \$21.

This elaborate textbook is the fifth edition in English and comprises 802 pages with 1,699 illustrations. Interestingly, all three volumes total 2,307 pages, which is over twelve times the size of the first edition on fractures published in 1929. The author has related 30 years experience in the management of these injuries and the work was of particular interest to the reviewer inasmuch as he enjoyed postgraduate course at Professor Böhler's Unfallklinik in 1955.

Impressions gained at that time of characteristic German efficiency adherence to established procedure and infinite attention to detail are reflected in this textbook.

There is an impressive statistical analysis of all the injuries from punch card records of 90 000 inpatients and 656,000 outpatients as well as roentgenograms of 256 000 cases. Typical case histories are used to emphasize teaching points and Doctor Böhler's wide experiences in the treatment of war wounds (two world wars) are recorded. Essentially he emphasizes the same principles of treatment as in his first edition. These include accurate anatomic reduction, use of the nonpadded plaster, sound wound surgery, avoidance of open reduction and use of the extremity during immobilization. Repetition and irrelevant verbosity detract from the volume and insufficient attention has been given to modern methods of open reduction and internal fixation, modern treatment of shock, use of antibiotics and newer anesthesia modalities for an authoritative textbook. Each section has a list of "Questions We Should Ask Ourselves to Avoid Failures With This Method." This is often obvious and tedious but always interesting. The appendix deals with education, organization and economic significance of traumatic surgery. The reader is given a splendid review of the accident problems in Austria and many of the thoughts can be applied to our own efforts in this country.

The material should be of interest to all clinical surgeons, especially those engaged in military orthopedic and traumatic surgery. The volume ranks with Watson Jones as a classic in fracture treatment.

—EARL W. BRANNON, Col USAF (MC)

ULCERATIVE COLITIS by Harry E. Bacon, B.S., M.D., Sc.D., LL.D., F.A.C.S., F.A.P.S. Foreword by Alton Ochsner, B.A., M.D., Sc.D., F.A.C.S., F.A.P.S. (Hon.) with contributions by Paul T. Carroll, B.S., M.D. Chapter on Anesthesia by Leroy W. Prumpman, M.D. 395 pages, 184 illustrations. J. B. Lippincott Co., Philadelphia, Pa. 1958. Price \$15.

This book is based on the author's experience with 440 cases of ulcerative colitis over a 17 year period and incorporates a substantial review of the literature. Every facet of the problem is thoroughly discussed. As one would expect, Dr. Bacon devotes considerable space to discussion of surgical treatment, including ileostomy, but it is noteworthy that one of the longest and best chapters is concerned with nonsurgical therapy.

The study of this perplexing disease must necessarily reveal diversities of opinion and experience. Dr. Bacon records these faithfully and without bias. The only apparent prejudicial note concerns those psychiatrists who incarcerate the patient for long periods of psychotherapy, frequently ignoring toxic symptoms and irreversible changes.

The text material is written in an informal, easily readable style. Rhetorical questions are used effectively to introduce controversial

topics. Particularly commendable are the photographs and listings of ileostomy appliances and accessories including prices and addresses of manufacturers or distributors.

There is little room for criticism of this book. There are a few minor errors in the text material certainly not excessive for a first edition. There is some duplication which might be eliminated. Some points of discussion are repeated perhaps for emphasis in subsequent chapters. A few photographs are reproduced twice. The placement of references at the end of each chapter results in multiple listing of reference material.

These imperfections are actually quite minor and do not detract from the excellence of this work. It is highly recommended for any one who is interested in the ulcerative colitis patient in any stage of his disease. —JAMES H. STEWART *Capt MC USN*

THE YEAR BOOK OF UROLOGY (1957-1958 Year Book Series) edited by William W. Smith, M.D. Philadelphia 359 pages illustrated. Third Year Book Publishing Company, Chicago, Ill. 1958. Price \$7.50.

This issue of the Year Book of Urology has again maintained its excellent presentations of the world literature on this subject. The selected articles are worth reading and very little extraneous material is included in the synopses from the original work. The chapter headings are the same as in previous years making it convenient to review entire subjects. The authors' notes at the end of some of the abstracts are very interesting and at times express an opinion entirely different than what was stated in the original paper.

It is gratifying to see more of the foreign literature included in this year's volume. The subject and author indexes at the end of the book are well arranged for easy and rapid reference identification.

This book is a must for the busy urologist who does not have the time to go through all of the allied medical journals on urology where many excellent articles on both clinical and research subjects are presented. It is a must for the resident who is preparing for his specialty boards as the material presented is up to date while most standard texts are several years out of date when first published.

—NICHOLAS MALLOS *Major MC USA*

FUNDAMENTALS OF ELECTROCARDIOGRAPHY AND VECTORCARDIOGRAPHY by L. U. Ellman, M.D. 142 pages illustrated. Charles C. Thomas Publishing Company, Springfield, Ill. 1957. Price \$9.50.

This monograph contains the basic fundamentals of electrocardiography and vectorcardiography. The opening chapter deals with fundamental vector concepts for which simple mathematical explanations are given. The next five chapters lay the solid groundwork for the chapters on the normal electrocardiogram and fundamentals of vectorcardiography. The use of the tetrahedral reference system and the more utilitarian hexaxial reference system is clarified. This is further noted.

grated into a spatial reference system by addition of the transverse reference system. Clarification of the mean spatial QRS-T angle is afforded together with a simple functional road mileage type of spatial QRS-T angle chart which can be mathematically proved and has been of inestimable value to me in studying borderline tracings. The clinical section is devoted to the problem of cardiac enlargement, conduction defects, pericarditis, myocardial infarction and arteriosclerotic heart disease, drugs and metabolism, arrhythmias and their interpretation. The book is laced with spatial vectorcardiograph models and related tracings which do not require a magnifying glass to read.

A perusal of this text serves to answer the query as to what vectorcardiography offers that is superior to routine electrocardiography. In problem and borderline electrocardiograms the use of the vectorcardiogram and force analysis of the standard tracings often give a clue as to the presence or absence of pathology. For those who profess an interest in cardiology and who feel a need to comprehend the flux of literature on vectorcardiography this book is commended. It is recommended that this book also be used as a reference for hospital libraries. —ARCHIE A. HOFFMAN, Col. USAF (MC)

**WORLD-ATLAS OF EPIDEMIC DISEASES** Part III. Second of four issues edited by Professor Dr. med. Ernst Rodenwaldt and Professor Dr. med. Helmuth J. Jusatz. Heidelberg, under the sponsorship of the Heidelberger Akademie der Wissenschaften. 32 pages, 10 maps. Volk-Verlag Hamburg. 1. January 1958. Price DM 63 plus extra charge for postage and packing.

This latest issue of the World Atlas like the previous ones presents a text in English and German concerning the clinical, statistical and geographic descriptions of specified diseases and the maps which comprise the atlas. As in previous issues the pages are not serially numbered but fit into the loose-leaf binder provided for Part III. Cholera (1931-1955) and Bacterial Dysentery in Asia (1900-1954) are the contributions to regional epidemiology. For Diphtheria (1934-1953), Poliomyelitis (1947-1955), Smallpox (1949-1955), Filariasis in Man (1955) and Trachoma (1930-1955) the scope is world wide. The plague pandemic of the twentieth century is documented and illustrated. Another significant addition to the climatological factors affecting populations, their health and welfare is included: the global regions of thermic suitability relate as usual to altitude.

The authors provide extensive bibliographies for each subject attesting to the thoroughness with which they have searched for reliable information. At the same time they are careful to define the limitations of their data. The work continues to be concise, lucid and precise.

The reader agrees wholeheartedly with those who have reviewed previous issues of this great work that it will make a most complete and authoritative reference. It is essential to the activities of public

health physicians military medical officers medical faculties and students as they contemplate the past and present in terms of disease and human ecology and as they make their plans for further studies and control effort —SIDNEY A BRITTEN C PL MC USN

HIGH ARTERIAL PRESSURE by F H Smith M D F R C P F R A C P 764 p g Illustrated Charles C Thomas Springfield Ill. 1958 P c \$15

*High Arterial Pressure* is among the most comprehensive and thorough volumes ever written on the subject. The author is well qualified to present the material covered in this book and he does so in an extremely readable style.

The physiology pathogenesis pharmacology and treatment of high arterial pressure are given complete coverage with treatment being given prime consideration. The author describes his approach to the evaluation of the patient his disease and treatment. He brings out the latest developments concerning all phases of the disease and presents his own views as well as those from the literature. The bibliography at the conclusion of each section is extremely complete and invaluable by itself.

This book is a very important contribution to the medical literature and is strongly recommended for all medical libraries. It will prove invaluable to the general internist and is a requisite for the cardiologist. Surgeons and general practitioners will find it useful for reference in the treatment of the hypertensive patient.

WILLIAM R SCHILLHAMMER M J MC USA

AUTONOMIC IMBALANCE AND THE HYPOTHALAMUS Imprint of Physiology Medicine Psychology and Neurophysiology by Ernest Gellhorn M D Ph D 300 p g Illustrated University of Minnesota Press Minneapolis Minn 1957 Pn \$8.50

In this monograph Dr. Gellhorn describes in some detail many of his experiments in which he has studied the sensitivity of the hypothalamus and the interaction between the hypothalamus and the autonomic nervous system and the central nervous system. They are presented in detail for workers who are research oriented. He discusses his concept of tuning of the sympathetic and parasympathetic branches of the autonomic nervous system and the way in which this state of being sympathetically tuned or parasympathetically tuned alters the response to subsequent stimuli. Dr. Gellhorn's ideas about the clinical implications of his work are exciting and bring us close to the hope of correlation between brain function and mental processes. He suggests that higher mental functions are related to definite alterations in neurophysiologic functions and that it may soon be possible to measure these alterations. There are many diagrams and an extensive bibliography of 330 references. This monograph will be of interest to all investigators in the field of psychophysiology. Clinicians will be interested in the summary and suggested clinical applications —ROBERT L WILLIAMS Lt C L USAF (MC)

THE MEDICAL MANAGEMENT OF CANCER by Henry D. Diamond M.D.  
F. A. C. P. 19 pages illustrated. Grune & Stratton Inc. New York  
N. Y. 1958. Price \$6.75

The author, a member of the staff of the Sloan-Kettering Institute for Cancer Research and the Memorial Hospital, has drawn from the experience in cancer diagnosis and therapy possible at such an institution together with a careful review of the literature.

For purposes of presentation the author has divided cancer into types for which the presently accepted mode of therapy is medical or nonsurgical and those types treated by surgical means. The first category contains the malignant lymphomas, the leukemias and plasma cell myeloma.

Despite the fact that at present there is no really satisfactory treatment for any cancer (except perhaps those of the skin which can be treated by large doses of x radiation) there are certain presently accepted forms of therapy which are beneficial at least in the sense of amelioration of many of the symptoms. This relatively small work admirably covers the highlights and many of the details of the symptoms, signs, diagnostic tests and therapy of the malignancies discussed. The role of the internist in the management of cancers in which primary treatment is surgical is also well covered. A short but adequate appendix on intracavitary application of radioisotopes is included.

This book is recommended to physicians who are concerned with the care of patients with cancer. The cancer specialist might find certain subjects for which he would desire a more extensive discussion of certain areas of controversy which are covered only in part. However, the large amount of material included in such a brief work makes this a readable and valuable book.

—NATHANIEL I. BERLIN Lt. Colonel MC USNR R

CURRENT THERAPY 1958 edited by Howard F. Conn M.D. 827 pages W.B. Saunders Co. Philadelphia Pa. 1958. Price \$12.

There are 297 contributors to this book, most of whom are well known authorities in their particular field. The consulting editors are outstanding teachers and clinicians.

The purpose of this volume is to give the practicing physician authoritative and current information on medical therapy. This has been achieved in an excellent, clear and concise manner. Most of the newer drugs and techniques of therapy are dealt with in a practical and helpful way—outlining both principles and details of therapy. It is reassuring to see that the recommendation for such drugs as the steroids and tranquilizers are kept in proper perspective by most contributors.

The contents include 16 sections which deal with infectious diseases, diseases of the various organ systems, of metabolism, allergic

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trated Paul B Hoeber Inc Medical Book Department of Harper &  
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Cabot R C. Pernicious and secondary anemia, chlorosis, and leukemia. In Oler W (editor). *Modern Medicine*. 3d edition. Lea & Febiger Philadelphia Pa. 192. Vol 5 pp 33-100

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*Head Stroke*

*Severe Dysbarism*

*High-Intensity Noise*

*Isolation of Vibrio Comma*

*Chelating Substances in Medicine*

*Primary Grafting for Psiloricidal Cysts*

SERVICE ARTICLES ☆ REVIEWS OF NEW BOOKS

CLINICOPATHOLOGIC CONFERENCE ☆ CASE REPORTS

# UNITED STATES ARMED FORCES MEDICAL JOURNAL

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UNITED STATES  
GOVERNMENT PRINTING OFFICE  
WASHINGTON 1958

## Monthly Message

Each spring there is a NATO Military Medical Conference which lasts three days. The 1958 meeting arranged by Major General William F. Powell USAF (MC) Chief of the Medical Section was held in Paris on April 1, 2, and 3. As an innovation this year the three days were divided with the first at Headquarters SHAPE, the second at the U. S. Air Base at Dreux, and the third at the French School of Aviation Medicine at Bretigny.

At the first session there was an address by General Norstad and briefings by his staff. In the afternoon the Norwegian group gave an excellent presentation of teaching methods including films and demonstrations by personnel, some so realistic that several in the audience thought they were true occurrences.

The meeting on the second day, the British, under the direction of Lieutenant General Sir Alexander Drummond RAMC, brought in a 100-bed surgical hospital by air and had it completely established, equipped and working with simulated patients within three hours. The group saw the arrival by air, the unloading of the airplanes, and then three hours later saw the hospital in full operation, even to the digging of latrine pits. In the afternoon the group inspected various types of U. S. transport cargo and medical evacuation aircraft on the base, witnessed the U. S. Navy demonstration, and saw a Turkish film of evacuation.

The third day was spent at Bretigny at the French School of Aviation Medicine with demonstrations by the group.

We returned to Paris and were entertained at the Val de Grace for lunch and during the afternoon. This has been the official military hospital of France since the days of Napoleon. The buildings date back about a century and a half to the first half of the 17th century when they were originally built as a convent.

Over one hundred delegates and guests were in attendance.

*Frank B. Berry*

FRANK B. BERRY M. D.  
Assistant Secretary of Defense  
(Health and Medical)

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## Foreword

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FRANK B BERRY M D

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S g G e r l U t d S t t A i r F

# UNITED STATES ARMED FORCES MEDICAL JOURNAL

Volume IX

August 1958

Number 8

## HUMAN TOLERANCE TO SOME OF THE ACCELERATIONS ANTICIPATED IN SPACE FLIGHT

STUART BONDURANT *Captain USAF (MC)*

NEVILLE P. CLARKE *Captain USAF (VC)*

WILLIAM G. BLANCHARD *Captain USAF (MC)*

HUGH MILLER *Captain USAF (MC)*

RUFUS R. HESSBERG Jr. *Lieutenant Colonel USAF (MC)*

EDWIN P. HATT M. D.

**R**ECENT technical advances have made human space travel imminent. The design of space vehicles and propulsion systems requires a comprehensive source of information concerning human tolerance limits to the accelerations which are expected. It is the purpose of this report to present a summary of the best current knowledge of these tolerance limits. This summary is based on published data and on studies which will be published shortly. For important details and comprehensive evaluation of specific points the individual reports should be consulted.\*

This report will treat only those linear accelerations which are expected during exit and re entry. It will not treat the zero g of orbital flight, nor will it cover the brief forces which may be generated in an emergency escape from the space vehicle or on impact landing.

F m A r M d l l b o r t r y W r g h t A r D e l o p m t C t e r W r i g h t P a t t e r n s  
A u t F e B s O h i W A D C T h c l R p o r t 58 156

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t o o c c u r d u r i n g e x i t a n d r e e n t r y f r o m s p a c e f l i g h t. T h e f o r c e s a r e e x p r e s s e d i n G  
u n i t s

## METHODS

All of the data presented here are based on determinations made on human centrifuges. The use of the centrifuge to produce acceleration introduces the artifact of angular acceleration of larger magnitude than that expected during exit and re entry. The possible significance of this artifact is treated in the discussion which follows.

Subjects in all tests were healthy young males experienced in riding the centrifuge. Rates of onset of acceleration were varied as indicated between 0.1 g and 8 g per second.

In most of the studies a plateau acceleration pattern has been used.<sup>1</sup> The acceleration was increased to the predetermined level which was maintained until a physiologic or an arbitrary end point was reached. The typical rocket profiles were not followed in these experiments because preliminary observations revealed no evidence of marked decrease in tolerance resulting from intermittent breaks in the acceleration pattern. The data should therefore be applicable to many anticipated acceleration patterns.

In some of the studies seated subjects have been exposed to forward acceleration patterns similar to those produced by a three stage rocket system.<sup>2</sup> These patterns consisted of successive accelerations to three instantaneous peaks of either 8, 10, or 12 g. After each peak deceleration was effected as rapidly as possible (20 to 35 seconds) to 1.5 g and the next acceleration begun immediately. The rate of increase of acceleration was constant throughout each run. It was selected so that if acceleration were stopped abruptly at the peak of each stage (as with most rockets) the total acceleration would be sufficient to increase velocity by more than 18,000 miles per hour. Because the centrifuge could not be stopped abruptly the subjects actually tolerated 15 to 25 percent more acceleration than required with an equivalent rocket pattern. In the series with three peaks at 12 g the rate of increase of acceleration was 1 g per 4.5 seconds; in the series with three peaks at 10 g the rate was 1 g per 7 seconds; and in the series with three peaks at 8 g the rate was 1 g per 12 seconds.

The duration of tolerance to accelerations of 6, 8, 10, and 12 g has been studied in semisupine subjects immersed in a tank of water on the centrifuge. Respiration was maintained under these conditions by delivering air for ventilation at a pressure equal to the hydrostatic pressure acting on the chest wall. This pressure was regulated by a skin diver's valve mounted under water at chest level.

The term tolerance limit as used in these studies indicates the point at which volunteer subjects were unable to withstand continued acceleration. The subjects were instructed to termi-

nate the acceleration when vision became seriously impaired (loss of peripheral lights), when respiration became impossible, or when pain reached an intensity which was estimated to be sufficient to impair judgment or performance. Experience with the centrifuge and motivation were thus unquestionably among the factors which determined the tolerance limits reported here. Within the stated tolerance limits, the subject would be expected to see, think, and exercise at least finger control. The accuracy of coordination and competency of judgment under these conditions remain to be evaluated.

### DATA

The curves of figure 1 are intended to approximate tolerance limits for 50 per cent of a young male population. The orbital velocity curve represents the time required at each g level to reach these velocities. This curve is included for comparison with the tolerance curves.

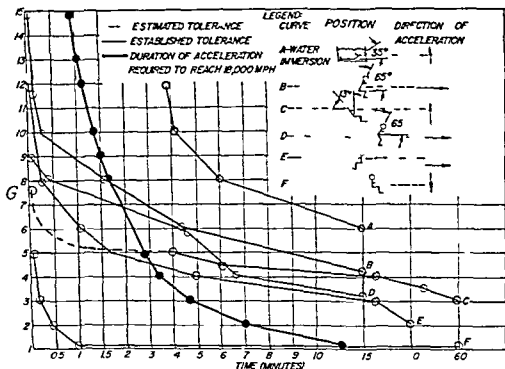


Figure 1 The duration of tolerance to acceleration

Certain considerations are of importance in determining the location of each of the tolerance curves.

#### Transverse G

In those positions (A, B, and D) in which the subject faces in the direction of acceleration, the angle of the trunk, relative to the direction of acceleration is critical. Tolerance to forward acceleration in the conventional seated position (fig. 2



B2) is limited at 8 g by dyspnea (difficult breathing) and chest pain. In addition, there is a component of negative G (footward acceleration) resulting from the backward tilt of the trunk. If the angle of the trunk relative to the direction of acceleration is greater than 70° (fig 2 B1) a severe quasi-pleuritic anterior chest pain limits tolerance at about 7 g. As the angle is de-



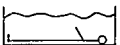












POSITION OF GREATEST TOLERANCE	DIRECTION OF ACCELERATION	POSITION OF LESSER TOLERANCE
 A (WATER IMMERSION)		 A
 B		 B1  B2  B3
 D		 D
 E		 E1
		 E2

Figure 2. Variation of tolerance to acceleration (vertical)

creased below 70° (fig 2 B3) there is a more longitudinal application of the inertial force (positive G) and blackout limits tolerance at progressively lower g levels (fig 2 B3). The best tolerances have been obtained with the subject leaning in the direction of acceleration at a 60° to 70° angle. Above 8 g blackout limit tolerance time in positions B (legs flexed) and D (semisupine) is greater in position B (12 g) than in

position D (10 g) was demonstrated by comparing the tolerance of the same subjects in the two positions (fig 1). This is assumed to be due to a greater displacement of blood from the legs toward the trunk in position B, an effect like that caused by an anti G suit. The tolerances in position D which are reported here are less than those reported previously.<sup>1</sup> The values obtained in the more recent study are used so that the relative merit of the two positions can be compared. The portions of these curves at and below 12 g are from work soon to be published.<sup>2</sup> The portions above 12 g are from other sources.<sup>3</sup>

In positions B and D, respiration becomes difficult above 4 g. Inability to maintain adequate respiration is the most common limiting factor at 6 and 8 g. Thoracic breathing is almost impossible at these g levels, and tolerance time is largely determined by the ability of the subject to practice abdominal breathing.

Above 6 g, petechiae of the back and the antecubital fossae occur consistently. The petechiae are usually not painful, do not interfere with performance, and are absorbed in two or three days.

In these positions (B and D), the subject is supported by the seat. Minimal restraint harness is necessary.

Disability after acceleration in these positions is variable. All subjects could make pertinent observations of the effect of the acceleration immediately after the run. Most were able to perform coordinated hand and arm movements before the centrifuge stopped. The accuracy of these movements was not tested. All were able to walk with an unsteady gait within a minute after acceleration. The unsteady gait, along with dizziness, vertigo, and occasionally, nausea persisted for one to five minutes after the run.

Tolerance of the seated, forward facing subject to backward acceleration (equivalent to the deceleration of re entry) is indicated in figure 1, curve E and in figure 3. Two factors are of importance in determining this tolerance limit.

First, the restraint system must be one which distributes the force evenly over large areas of the body without pressure points or local vascular occlusions. The tolerances indicated here were obtained with a suit designed to meet these requirements. Current operational harnesses are not adequate. A maximum of 5 g was tolerated with several harnesses basically similar to the U. S. Air Force integrated harness.

Second, the position of the body must be as indicated in figure 1 E. If the head is allowed to move forward during acceleration (fig 2, E1) an effective negative G component is introduced. The greater the forward movement of the head, the lower is the

tolerance. If the legs are extended (fig 2 E2) intense calf and thigh pain limits tolerance at about 5 g. This pain may persist for several days. It is assumed to be related to the local vascular distension and high pressures which occur with backward acceleration in this position. Wrapping the legs with elastic bandages and voluntary tensing of the leg muscles ameliorate the pain somewhat, but these techniques have not measurably improved tolerance in position E<sup>2</sup>.

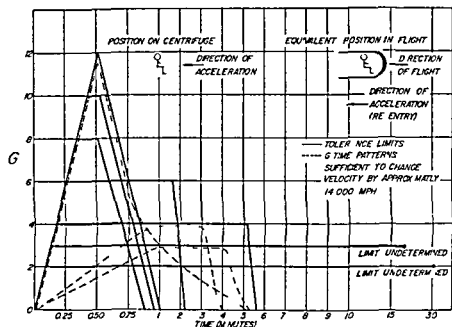


Fig. 3. Tolerance of backward acceleration in flight (1 g).

In the optimal position for backward acceleration (fig. 1 E) tolerance to accelerations of 4 to 8 g is generally limited by leg pain similar to that described above. At levels above 8 g, both leg pain and dyspnea have been limiting factors. Petechiae occur consistently over the hands and anterior legs at high g levels.

Residual effects of acceleration in position E have been essentially like those described above for positions B and D.<sup>1</sup>

#### Position G

The seat used in the studies of positive G tolerance has a 10° backward tilt of the backrest. The subjects sat with legs partially extended.

Headward acceleration can be tolerated by the subject in this position without an anti-G suit for the times indicated in

figure 1, curve C, if the rate of acceleration to each g level is approximately 0.1 g per second. At higher rates of acceleration, an anti G suit may be required by some subjects. Since the subject is supported by the seat, minimal restraint harness is necessary. Petechiae occur commonly over the legs, feet, and lower arms after more than 10 minutes above 3.5 g. Tolerance in this position is generally limited below 4 g by fatigue, backache, and headache.

Because of the slow rate of onset of acceleration, blackout is rare below 4 g. It is the limiting factor in many subjects at 4 to 5 g. Occasional episodes of profuse sweating, pallor, nausea, tachycardia, and a sensation of imminent loss of consciousness have occurred in this position without relation to the magnitude or duration of the acceleration. Acceleration was stopped immediately in each instance. Weakness, dizziness, malaise, and nausea often persisted for several hours after these episodes.

Residual effects after headward acceleration for the times indicated in figure 1, C, are highly variable among subjects, and for the same subject on different days. Residual effects may be as slight as those described for positions B and D above, or weakness, dizziness, and malaise may be prostrating for several hours.

### Negative G

The tolerance curve for footward acceleration refers to the seated subject (fig. 1, F). The upright subject would probably be less tolerant of negative G. Protective devices (pressure helmets) can be used to increase this tolerance limit. Even so, this is the position of least tolerance. Tolerance time is generally limited by head and eye pain. Subconjunctival hemorrhages and transient cardiac arrest have been reported.<sup>10</sup>

### Water Immersion

Water immersion (fig. 1, A) allows tolerances at least as great as those indicated. The angle of the trunk, relative to the direction of acceleration, is critical whether the subject is in water or in air. The 35° angle indicated in position A, figure 1, seems to be optimal for the immersed subject. Restraint of the immersed subject is unnecessary. Petechiae do not occur during acceleration to 12 g with the subject immersed. Among the advantages of water immersion is the freedom of movement of the subject regardless of the g level. The freedom with which the head can be moved at high g levels makes labyrinthine stimulation likely and vertigo a potential problem. If the head is held in one position, dizziness is only moderate, persisting for one to five minutes after acceleration.<sup>2</sup>

### Rocket like Acceleration Patterns

Figure 4 presents three three stage rocket like acceleration patterns which have been tolerated by a small group of subjects in position B. The residual symptoms after these accelerations were highly variable. All subjects were able to talk and to move arms and legs before the centrifuge stopped. Crude tests of coordination of the hands and arms were performed within one minute after acceleration. No marked deficit was observed. Some subjects experienced marked malaise and dizziness for five minutes to one hour after acceleration. In this small series these symptoms were observed mostly in inexperienced subjects.<sup>2</sup>

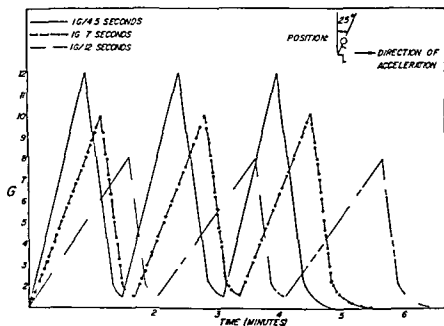


Figure 4. Some of the best rocket acceleration patterns tolerated in position B. The acceleration was 1G for 4.5, 7, or 12 seconds.

No tests of performance were made during any of these accelerations. However, in agreement with previous reports it was observed that arm and leg movements are not highly effective at more than 6 g (unless the subject is immersed). Wrists and fingers could be moved at all g levels in all positions.

### DISCUSSION

#### Exit Acceleration Patterns

Acceleration of the magnitudes and durations anticipated during exit from the earth's atmosphere can be tolerated without anti-G equipment in at least two positions (B and D). Of these two positions, the former (position B, seated) has two advantages.

tolerance is greater by approximately 2 g, as tested on the same subjects and a smaller top to bottom cabin dimension is required to accommodate the subject. This position has the disadvantage of being rather uncomfortable for long periods of time when there is no forward acceleration. An adjustable seat back would be required to enable the necessary forward tilt during forward acceleration and the more comfortable upright position during flight. Deceleration would be poorly tolerated by the subject in positions B or D, because the forward tilt would introduce a negative G component. For this reason, in either position there should be provision for immediate return to the upright position in the event of emergency deceleration during the boost phase and during re entry.

At high g levels (above 8 g) blackout or dyspnea limit tolerance in positions B and D. Blackout occurs because of the effective positive G associated with the tilt of the trunk in the direction of acceleration. Blackout caused in this way is subjectively indistinguishable from that associated with the usual positive G and, like the latter, can be forestalled with appropriate straining maneuvers. Dyspnea can be partially overcome by the practice of abdominal breathing. Even with this technique, when acceleration exceeds 10 g, the effort required to breathe is so great that it could be maintained by these subjects for only a few seconds (fig. 1).<sup>3</sup>

Of particular interest are the rocket like acceleration patterns of figure 4. With most liquid fuel rockets, the rate of acceleration increases more slowly at first and more rapidly just before burn out. These patterns result in longer times at low acceleration and shorter times at high acceleration than the experimental patterns with a constant rate of increase of acceleration. The actual rocket acceleration pattern would therefore be expected to be better tolerated by man than an equivalent pattern of the experimental type.

Rather than attempt a reproduction of specific rocket acceleration patterns, as reported in a previous study,<sup>3</sup> the pattern of least tolerance (a constant rate of increasing acceleration) was used in this part of the study. Any actual rocket acceleration pattern which fits within these limits should be tolerated. Further, since the forward facing subject can tolerate forward acceleration of 4 g for longer than 15 minutes, only those portions of the actual rocket acceleration curves which lie above 4 g need be considered. If these portions of the actual patterns lie within the portions of experimental curves (fig. 4) which are above 4 g the pattern would be expected to be tolerable regardless of the time required to reach 4 g. Since three peaks of 12 g are tolerable, any combination of three of the individual stages illustrated here would be expected to be tolerated and would achieve a velocity in excess of 18 000 miles per hour.<sup>3</sup>

### Re-entry Acceleration Patterns

The magnitude and duration of deceleration associated with re entry into the earth's atmosphere will depend primarily upon the angle of entry and the aerodynamic characteristics of the vehicle. In general, a large angle of entry and/or a low lift/drag ratio of the vehicle result in a large force acting for short periods of time while a small angle of entry and/or a high lift/drag ratio result in a small force acting for longer periods of time. Representative  $g$  time curves of each type are illustrated in figure 3.

The deceleration of re entry can be tolerated in several positions. If adequate restraint is available, the low  $g$  (less than 4  $g$ ) long duration patterns are tolerable in any position except head forward (negative  $G$  position F). High  $g$ , short duration forces are best tolerated in position E, B, or D. Early studies indicated a superiority of position D so great as to justify rotating the pilot 180° to face aft during the re entry period. In this way the forces of re entry would be oriented in the same direction as those of exit with respect to the pilot and to the seat. More recent studies have indicated that with adequate restraint the seated forward facing pilot (position E) can tolerate decelerative forces of the same order of magnitude (fig 1) as the seated aft facing pilot (position B) or the semisupine aft facing pilot (position D). This observation was to be expected since tolerance to transverse acceleration is essentially the same in the prone and supine positions.

It would therefore appear that rotation of the pilot to face aft during re entry might be unnecessary in some patterns. It must be re emphasized that tolerance of the seated forward facing pilot to deceleration is determined largely by the efficacy of the restraint harness. The ideal harness constitutes a support equivalent to a firm outline of the body of the subject.

### Prolog and Positive Acceleration

There have been few systematic investigations of the duration of tolerance to positive acceleration. The data summarized in curve C, figure 1, exceeds previously reported limits by a wide margin. These tolerances were demonstrated by employing a rate of onset of acceleration which was slow enough to allow reflex cardiovascular compensatory mechanisms to come into full force before maximum acceleration was reached. A faster rate of onset results in blackout at the usual  $g$  levels unless an anti  $G$  suit is used. These observations indicate that velocities in excess of 18 000 miles per hour may be reached by headward acceleration of the seated subject if the magnitude of acceleration does not exceed 5  $g$ . For instance, an acceleration of 3  $g$  maintained for one hour (figure 1, curve C) would increase velocity by 935 000 miles per hour.

### Water Immersion

Preliminary observations suggest that the duration of tolerance of immersed subjects to acceleration up to 12 g is in excess of twice the maximum reported for nonimmersed subjects. Since, as indicated in figure 4, water immersion is not required to tolerate accelerations sufficient to reach orbital velocity, the usefulness of this protective technic is questionable. The tolerance of the immersed subject to acceleration in excess of 12 g has not been investigated.

### General Considerations

The rate of increase of acceleration is of some importance in determining both positive and transverse acceleration tolerance.

With transverse acceleration, rates of onset faster than those indicated have resulted in slightly longer (few seconds) tolerances at high g levels. Slower rates of onset have shortened the time of tolerance.<sup>3</sup> The same considerations apply to slower rates of onset with positive acceleration as with transverse acceleration.<sup>4</sup>

In addition to the data summarized in figure 1, it has been reported that 15 g can be tolerated for five seconds in position D if the rate of increase of acceleration is 6 g per second.<sup>4</sup> It appears doubtful that this rate of increase of acceleration will be encountered other than during an emergency. During World War II, two subjects tolerated 17 g for one minute on a German centrifuge. The subjects were in position B. The maximum rate of increase of acceleration possible in this instance was 1 g per 6 seconds. The subjects were reported to have been ill for an indefinite period after the experience. There were no permanent residua.<sup>5</sup> It would appear, therefore, that the tolerance limits indicated in the current studies are well below the level of injury.

A general characteristic of all the curves of figure 1 except F is the excess tolerance at low g levels, in all positions, over that required to reach orbital velocity. A larger g time product (greater velocity) can be reached by low g for long periods of time than by high g for short periods. Prolonged low g (below 4) therefore, constitutes one means whereby man can reach velocities in excess of those required for orbit or escape. Arm and leg movements can be effective at these low rates of acceleration.

Although there have been no measurements of performance during the studies summarized here, certain observations are pertinent. A study of the ability of subjects to perform a dual tracking task during three stage accelerations to peaks of 8, 5.8 and 5.8 g has been reported. The decrement in tracking



ability was so slight that the authors concluded that select crewmen can be expected to assist in the control of such a vehicle during the critical acceleration phases of the flight. It is generally recognized that highly effective arm movements cannot be executed above 6 g. Wrist and finger movements can be executed up to at least 12 g.

The importance of the post-acceleration symptoms as observed in these studies cannot be established. A few of the subjects consistently presented minimal post acceleration symptoms. Others consistently presented maximal symptoms and in still others the symptoms varied from day to day. In no instance was a subject incapacitated even immediately after acceleration.

The use of the centrifuge to produce acceleration introduces the artifact of angular acceleration of larger magnitude than that expected during exit and re entry. The effect of this artifact is to increase stimulation of the labyrinth. In none of the accelerations reported here were the runs limited by symptoms of labyrinthine stimulation. It is therefore the opinion of the authors that this artifact did not significantly modify either the magnitude or the duration of the accelerations which were tolerated. After acceleration on the centrifuge manifestations of labyrinthine stimulation were consistently present (dizziness, vertigo, nausea and occasionally nystagmus). It is possible that the post-acceleration symptoms were due at least partially to angular acceleration. This premise is supported by the observation of many of the subjects that the symptoms began during the period of deceleration<sup>1</sup>. It would seem safe to conclude that the post acceleration symptoms after linear acceleration would not be more severe than those encountered in these studies.

### SUMMARY

Human tolerance limits to the major linear components of the acceleration patterns anticipated in achieving space flight have been reviewed. Acceleration of the anticipated magnitude and duration is best tolerated with the body positioned so that the forces act transversely in a chest to back or back to chest direction. The optimal body position for exit appears to be a seated position with a 90° inclination of the trunk in the direction of acceleration with the legs fully flexed (seated forward facing). Three stage accelerations sufficient to reach orbital velocity with peaks of either 8, 10, or 12 g are tolerable in this position. With the trunk in the position described in paragraph 3 but with the legs partially extended perpendicular to the direction of acceleration (semi supine position) acceleration peaks to 10 g are tolerated. Such acceleration patterns are also sufficient to reach escape velocity.

Some of the patterns of the deceleration of re entry can be tolerated in the seated, forward facing position with the aid of an effective restraint system. Tolerance would be only slightly improved by rotating the subject to face aft during re entry. Accelerations of less than  $4 g$  are tolerable in either chest to back, back to chest, or foot-to head direction for long enough to exceed escape velocity. Prolonged low  $g$  acceleration patterns, while not feasible with current propulsion systems, have the potential advantage of enabling man to reach very high velocity (200 000 m p h) and to retain a degree of mobility sufficient to perform limited control functions during the boost phase. Immersion of the entire subject in water enables the attainment of tolerance times greater than twice those reached in any other way. The full possibilities of this method of protection have not been explored.

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## HEAT STROKE

JEROME FABRICANT C pt MC USA

**T**HE EMERGENCE of homeothermic animals was a major evolutionary event in that it greatly liberated the animal from its environment. This was accomplished by a thermoregulatory mechanism which maintained a narrow range of body temperature despite wide swings in environmental temperature. In contrast the cold blooded animal whose tissue temperature approaches that of the outer world remained a slave to its environment. The tempo of its activity was largely dictated by the whims of environmental temperature.

Temperature constancy is dependent upon a balance between the heat gain and heat loss of the body. Heat gain is caused by metabolic activity and in hot climates radiation convection and conduction of heat to the body. Heat loss occurs principally by the evaporation of water from the skin and surfaces of the respiratory system. In temperate climates considerable heat loss also occurs by radiation and convection of heat from the body. The remarkableness of man's heat regulating mechanism was dramatically demonstrated in 1775. It was then shown that a man could withstand a temperature of 250 F in an oven for 15 minutes without any ill effects or serious rise in body temperature. Yet a beefsteak was cooked in 13 minutes at the same temperature.

The heat regulating mechanism can be strained or interfered with during prolonged exposures to heat so that heat casualties will result. The number of victims can reach epidemic proportions to the point of disrupting military operations. For example during the summer of 1942 two armored divisions were transported on air conditioned trains to a desert training site. The daily temperature range of the area was approximately 88 F to 120 F. One division arrived in the latter part of July and immediately set up camp. The incidence of heat casualties was considerable. It was not uncommon that 20 to 30 victims a day were admitted to the hospital. On one day alone 150 victims were admitted. There were however a larger number of casualties who were not admitted but were nevertheless ill enough to be rendered unfit for duty. The division as a whole had become ineffective and could have been an easy prey for the enemy.

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F m l r l d Army H p t l F r t K Ky

The other division began to arrive in the same area two weeks after the first. The incidence of heat illness was markedly reduced because of the experience gained in the handling of the first.

### Incidence

Heat stroke is the most serious of the heat disorders, with reported mortalities of 10 to 80 per cent.<sup>8</sup> Other forms of heat illness—heat syncope, heat exhaustion, heat cramps, and thermogenic anhidrosis—are rarely, if ever, fatal.

In a civilian population most of the heat stroke victims are in the upper age group, with associated general and cardiovascular arteriosclerosis. In the military most victims are basic trainees, less than 30 years of age, often transferred from their homes in the north to southern training sites.<sup>9</sup> Malamud, Haymaker, and Custer, in a series of 125 fatal cases of heat stroke in the military between 1941 and 1944, noted that one quarter of the victims had been in the Army less than two weeks, and about one half for less than two months.

There have been scattered reports of iatrogenic heat stroke in hospital patients.<sup>7, 10</sup> These were often surgical patients who had been prepared for surgery or endoscopic examination with NPO orders, atropine (which suppresses sweating) and barbiturates (which inhibit the heat regulating center). In a non air conditioned operating room, in a patient wrapped snugly in gowns and the sheets of the operating table, evaporative and convective heat loss are effectively screened.

Outbreaks of heat stroke are also reported in geriatric and mental institutions.<sup>9</sup> In July 1954 the Midwest suffered a heat wave with temperatures rising above 106 F for 14 consecutive days. On 13 July, with a temperature of 116 F, a Kansas mental institution began having an outbreak of heat illness which included 25 heat stroke cases. Three of these or 12 per cent died.

### Pathophysiology

In some victims, heat stroke seemed to occur precipitously without premonitory symptoms. Yet few heat stroke casualties appeared during the early part of a heat wave.<sup>8</sup> Apparently there was a subclinical build up of abnormal physiologic processes within such victims. Existing literature on heat stroke refers to the possibility of a failure of the heat dissipating center of the hypothalamus. The anterior portion of the hypothalamus contains neurons, susceptible to rising blood temperature and afferent impulses from the peripheral thermoreceptors.<sup>10</sup> The descending pathways of the hypothalamic center pass down the brain stem and set up connections with respiratory and cardiovascular mechanisms of the brain stem and spinal cord. Under conditions of heat exposure, the center evokes increased respiration to the stage of panting and increases peripheral blood flow and perspiration.

It is also possible that an inhibition of metabolic heat production occurs

Lesions of the anterior hypothalamus such as tumor infection hemorrhage and trauma, can cause inability to adjust to elevated external temperature. It is not uncommon that the body temperature rises to 105 F to 107 F in the terminal stages of cerebral hemorrhage and after surgery for craniopharyngioma.

In view of its important role in body temperature regulation the hypothalamus has been examined in fatal cases of heat stroke. Malamud, Haymaker and Custer, however, were unable to demonstrate significant anatomic change in the hypothalamus of 125 fatal cases of military age. This was in contrast to other portions of the brain, especially the cerebellum, which displayed much greater damage in the form of hemorrhage, edema, reduction of neurons, and increase of glial elements. Apparently the damage within the hypothalamus was on biochemical/biophysical levels well beyond the range of the microscope.

The biochemical defect may well be in the nature of a central nervous fatigue. Fatigue refers to the inability of nervous tissue to maintain a maximal excitatory state.<sup>1</sup> The nature of such fatigue is largely unknown. Central nervous system fatigue might result from several causes, such as the using up of energy-producing materials, depletion of humoral transmitters at synapses, and accumulation of wastes that block nerve transmission.<sup>1</sup> The concept of fatigue can be used as part of a working hypothesis in the pathogenesis of heat stroke. One may picture the hypothalamus under maximal stimulation during exposure to prolonged and severe heat stress. The hypothalamus must constantly evoke the peripheral processes that promote heat loss: maximal sweating, increased peripheral blood flow, and respiration. Should any of the peripheral heat-loss mechanisms be defective, as for example, the congenital absence of sweat glands, or defective sweating resulting from previous brain damage, the hypothalamus is placed under a greater strain than usual and is more readily subject to fatigue.

The hypothalamic fatigue is probably progressive and is reflected peripherally in a gradual diminution of sweating. Many heat-stroke victims note a defective sweating hours or days before the onset of severe neurologic symptoms. Gerking and Robinson demonstrated a 10 to 80 per cent decline in the sweating rate during 6-hour exposures of working men to severely hot environments. The decline was greater in wet than dry heat. Kuno,<sup>2</sup> commenting on these experiments, noted that the sweating rate was rapidly restored with lowering of body temperature under laboratory conditions. He did not believe that this could occur with a peripheral fatigue of the sweat-secreting cells. Patler, the decline was probably caused by a disorder in the nervous system.<sup>3</sup>

Ladell<sup>14</sup> also found a falling off of sweat response in an exponential manner with constant skin temperature and rising rectal temperature. After a certain temperature was reached, any further rise in temperature resulted in a decrease in total sweat production. Theoretically, at a rectal temperature of 110 F, the sweating rate is practically nil. Inasmuch as the fall in sweating rate is rapidly reversible, he also did not believe that it was a true fatigue. Ladell concluded that the cessation of sweating in hyperpyrexia is intrinsic in the nature of the sweat gland response and that there was no need to postulate any pathologic process. He believed that heat stroke is "a purely physiological phenomenon." This is probably an over simplification. It should be noted that the sweat gland response has a nervous component. The rapid reversal of sweating rates is not inconsistent with a fatigue of the central nervous system centers. One may consider the fatigue as "physiological" in that it is an intrinsic property of the nervous tissue taking part in the sweating response. This seems to be, however, a purely semantic problem. One can call pneumonia "a purely physiological phenomenon" in that it is intrinsic in the nature of lung tissue to undergo inflammation when invaded by certain organisms. In addition, Ladell's experiments were done with healthy men under controlled conditions and were fairly acute in time, usually a matter of a few hours. Heat stroke victims, however, are usually exposed to excessive heat loads for several days before the overt manifestation of their illness. Furthermore, a rapid restoration of sweating with a drop in rectal temperature does not always occur in actual heat stroke victims.

With this background in fatigue, the following sequence of events is postulated: (1) The victim is exposed to an excessive heat load which tends to raise the body temperature. (2) The excessive stimulation tends to fatigue the hypothalamic center. (3) The sweating rate gradually diminishes and the body temperature rises further. (4) Body metabolism is accelerated by the elevated body temperature, thereby producing further heat in the body. (5) Shock ensues as the result of heat damage to the vasomotor centers. The peripheral vasoconstriction accompanying the shock further impairs heat loss. (6) The hyperthermia damages the brain and other organs. Hyperthermia and the anoxia of shock lead to the death of the victim.

There is little mention made in the literature of the mechanism of heat death on the cellular level. Yet this is an important consideration in that the symptomatology and lethality of heat stroke can be traced to the direct effects of heat upon the cell. Most of the work on cellular heat death has been done with unicellular organisms, plants and cold blooded animals.<sup>15</sup> The findings may supply clues as to what occurs in human heat stroke casualties.

Examination of heat killed cells reveals an increased viscosity of the protoplasm. From this it is assumed that heat kills by

directly causing an irreversible clotting of protoplasm or destruction of the cell enzymes or both. Plants and animal cells however can be killed at temperatures which do not cause irreversible protein coagulation or enzyme destruction.<sup>7</sup> Furthermore there were heat stroke victims whose temperatures never reached above 103 F to 104 F.<sup>1</sup> It seems unlikely that such temperatures can cause irreversible protein coagulation or enzyme destruction. Heilbrunn suggested that heat death is initiated by the action of heat on the cell lipids. The melting point of fats probably has something to do with heat acclimatization. Animals and plants of the tropics have higher melting point fats than those in northerly climates. The melting point of fats can be raised by subjecting an animal to chronic heat exposure. This has been demonstrated in insects, fish, plants, pigs and other organisms. Furthermore the melting point of fats has been correlated with heat resistance—the higher the melting point the more resistant the animal is to heat stress.<sup>17</sup> Whether the above also applies to humans is not known. If we assume it does then soldiers could conceivably be made heat resistant and less prone to heat illness prior to entering hot climates. This could be done with diets containing solid fats and carbohydrates which tend to raise the melting point of body fats.

Heilbrunn believed that excess heat tends to dissolve or liquefy fats—especially those with relatively low melting point—situated in the cortex of the cell. As a result there is a loosening of the chemical bonds between calcium and fat so that an excess of calcium is released into the interior of the cell. The calcium causes severe clotting of protoplasm and death of the cell. Fat solvents such as ether and alcohol have the same effect as heat. This then suggests that alcohol can augment the effect of an excessive heat load and thereby predispose one to heat stroke.

The question arises as to why certain individuals in a group exposed to the same heat load are the only ones affected. Could there be some predisposing abnormality in the means of heat dissipation? It is interesting that some heat stroke victims stated that they rarely if ever perspired.<sup>1</sup> This then suggests the possibility of an abnormality in the sweating mechanism. The congenital absence of sweat glands is an obviously predisposing factor but such cases are rare. One wonders whether there is a relative diminution of sweat glands in those prone to heat stroke. There are racial differences in the number of sweat glands, the Negro having more than the Caucasian. Kuno found a considerable variation among the Japanese. In a study of seven Japanese the average number of glands per sq cm varied from 143 to 339. Furthermore there was some correlation between the amount of sweat emitted and the size of eccrine sweat glands. Conceivably a congenital atrophy of sweat glands in addition to subnormal numbers could predispose one to heat illness.

There has been, however, no systematic study of the sweat glands in heat stroke victims

There are cases on record in which the number of sweat glands was normal, but their functioning was defective.<sup>18</sup> These cases may have had previous brain damage in the form of an encephalitis in childhood. A careful search of the medical history of victims may reveal the occurrence of childhood febrile convulsions, or other abnormal neurologic occurrences, which could account for a functional disorder of the hypothalamic heat dissipating center.

Chronic degenerative disease may also predispose to heat stroke. Morgan and Vonderahe<sup>19</sup> studied the hypothalamic nuclei in 13 elderly victims and compared them to the hypothalamus of cases not associated with heat stroke. They found a diminished number of cells in the anterior nuclear groups—which are concerned with heat loss—that are apparently the result of previous disease. The posterior groups—concerned with heat conservation—had normal numbers of cells that showed acute pathologic alterations. The normal balance between heat loss and heat conservation probably was tipped in favor of heat conservation in those victims prior to heat stroke. With excessive heat stress, the anterior nuclei were thus unable to evoke sufficient heat dissipation because of previous damage. The pathologic alterations in neurons of the posterior nucleus suggested intense over activity. Possibly there was a lessening of normal checks and inhibitions to the extent that heat production and conservation were accelerated rather than inhibited. The findings of Morgan and Vonderahe are at variance with Malamud, Haymaker, and Custer<sup>6</sup> who found no significant anatomic changes in the hypothalamus. The probable reason is that the latter studied specimens from young men of military age, and the former used material from victims over 50 years of age, who had had chronic degenerative disease (chronic vascular sclerosis, syphilis, or chronic alcoholism).

The degree of hydration may be an important variable in pre disposition to heat stroke. Lichten,<sup>21</sup> working with subjects acclimatized to heat for 2 weeks, demonstrated that there was a rise in the threshold for sweating and also a fall in the rate of sweating in acute water deprivation. The rectal temperature in the dehydrated subjects reached high levels at much lower effective air temperatures than was the case in normally hydrated subjects. Dehydration is said to set the hypothalamic thermostat at a higher than normal level,<sup>22</sup> therefore adding to the vicious circle of hyperpyrexia.

Obesity makes an individual more prone to heat stroke.<sup>23</sup> Death because of hyperthermia is three and one half times more likely among those who are 40 lbs overweight than among individuals who are overweight by only 10 lbs.<sup>23</sup> Inasmuch as metabolic heat



is produced proportionately to bulk of tissue and is lost proportionately to surface area, a low volume to-area ratio is a great liability in a hot environment

In a series of 74 patients 23 or 30 per cent gave a history of alcoholic intake prior to the onset of heat stroke. Five subsequently died. Alcohol stimulates the sweating mechanism through its central action.<sup>1</sup> Conceivably such an added stimulus to an already overburdened hypothalamus may in part be responsible for its failure.<sup>2</sup> However the work of Heilbrunn, discussed above, suggested that alcohol augments the effect of heat by its action on cell lipids.

There are then several abnormalities that may predispose one to heat stroke: abnormalities in number and size of sweat glands; previous hypothalamic damage resulting from encephalitis; febrile convulsions; chronic degenerative disease; et cetera; acute water deprivation; obesity; acute alcoholism; and abnormal fat metabolism.

The absence of abnormal anatomic or physiologic predispositions make the occurrence of heat stroke less likely. Heavy physical work, improper clothes, high humidity, excessive radiant heat loads, et cetera, can also in and of themselves lead to heat stroke.

### Clinical Features

In Austin and Berry's series of 100 cases, only 7 per cent stated that their symptoms began suddenly. 28 per cent had symptoms for less than 24 hours. The majority had premonitory symptoms lasting 2 to 5 days. In a series of 125 fatal cases, 71 per cent were acute without warning. 91 per cent had prodromata of a few minutes to hours, and 8 per cent had symptoms lasting several days prior to heat stroke.

Prodromata, in the order of their frequency,<sup>4</sup> were faintness, staggering gait, dizziness, headache, nausea and vomiting, purposeless movements, muscle cramps, choking, difficulty in swallowing or speaking, numbness of extremities, drowsiness, restlessness, mental confusion, dryness of the mouth, excessive thirst, anorexia and diarrhea. Three to four per cent gave a history of previous heat illness.

Death occurred within 24 hours in approximately 70 per cent of 125 fatal cases; the remaining surviving as long as 12 days. Of the 17 deaths in Austin and Berry's series, 7 occurred within 24 hours, 7 within 1 to 6 days, and 3 within 6 to 13 days. The cause of death was acute left ventricular failure in 8 of 17 fatalities, and uremia in 2. The remaining 7 deaths resulted directly from the effects of heat.

The temperature of a heat stroke victim does not necessarily rise above 106 F. Such cases have been termed borderline

hyperthermia" by Luc Li Fu et al. and Harrison.<sup>2</sup> Of 100 cases, 37 were never associated with temperatures over 106° F. 10 per cent of these died in contrast to a fatality of 27 per cent in victims with temperatures above 106° F.

Patients seen initially with subnormal or slightly elevated temperatures usually showed a subsequent rise to levels exceeding 107° F. After the hyperthermia is reduced by some cooling measure, there is often a secondary rise or several rises in temperature—probably an indication of the instability of the hypothalamic center.

In a study by Malamud, Haymaler, and Custer, blood pressure was normal in 35 per cent of 55 fatal cases. The remainder had systolic pressures ranging from 40 - 100 mm Hg and diastolic 0 - 60 mm Hg. The presence or absence of shock levels was a better prognostic index than the degree of hyperthermia. In cases in which survival was longest, shock was either successfully controlled at the very onset or was not appreciable until the terminal stages. Approximately one third of those with systolic pressures below 100 mm Hg will die.

The work of Davis and Harrison<sup>2</sup> on experimental heat stroke in animals suggested that initially an excessive heat load caused a cutaneous vasodilation with compensatory splanchnic vasoconstriction. The shock in heat stroke occurs when the vasomotor centers, incapacitated because of thermal injury, fail to affect the compensation. In addition, the splanchnic vessels may dilate as a result of the direct stimuli of heat or acid metabolites, or both.

Complete or marked suppression of sweating is one of the cardinal manifestations of heat stroke. This finding is important in differentiating heat stroke from other diseases. Occasional victims, however, show hyperhidrosis.<sup>6, 22</sup> This may be because of the co-existence of heat stroke with heat exhaustion in which heavy perspiration is the rule.

Disturbances in consciousness from lethargy to coma are usual. Only 2 per cent exhibited normal levels of consciousness.<sup>6</sup> There may be generalized or Jacksonian type convulsion, muscle rigidity or flaccidity, meningeal signs, pyramidal sign, opisthotonos and decerebrate rigidity. The higher the temperature, the more severe the central nervous system signs.

Neurologic sequelae, particularly of the cerebellar type, are not uncommon in heat stroke survivors.<sup>23</sup> In 1 of 20 survivors, or 5 per cent, cerebellar symptoms persisted.<sup>6</sup> There may be ataxia, nystagmus, incoordination of the extremities, athetoid movements, speech disturbances, irritability, headache, psychosis, apathy, disorientation, hemiplegia, etc.

Other possible accompaniments of heat stroke are jaundice, pneumonia, muscle cramps and tetany, uremia, anuria, and purpura.<sup>6</sup>

### Laboratory Findings

In a study of 15 cases<sup>7</sup> an initial hemoglobin of 11.6 to 16 grams per 100 ml (average 13.6) was found. This decreased in one week to 8.2 to 13.8 (average 10.7). There was no obvious blood loss. An increased rate of red blood cell destruction was detected in 10 patients. According to Iadell, Waterlow and Hudson, hemodilution is usual in the later stages of heat stroke because water accumulates in the body upon cessation of sweat in<sub>g</sub>. White blood cell counts were normal or elevated.

Thrombocytopenia was present in all cases. In 6 fatal cases there was a progressive fall in platelets, but in one there was a return to normal values before death. Prothrombin time may be normal or prolonged, probably as a result of liver damage. Prolonged clotting time was found in 5 of 15 cases.<sup>7</sup> The impaired coagulation of blood accounts in part for the widespread hemorrhage found at autopsy.

Wright, Reppert and Cutting<sup>2</sup> demonstrated capillary fragility by means of the tourniquet test. They suggested that the capillary dilation that occurs on exposure to heat may reach a pathologic state permitting red blood cells and plasma to extravasate. They postulated that in addition to a decrease in prothrombin time or platelet count or both, capillary damage contributes to the purpuric manifestations of heat stroke.

Blood urea nitrogen determinations were performed in 61 patients. 29 showed blood urea nitrogen above 20 mg per cent. 9 deaths occurred in this group, indicating the seriousness of this finding. Elevated blood urea nitrogen may not necessarily reflect kidney damage, but rather generalized tissue destruction.

In heat stroke, blood electrolyte levels were usually not remarkable unless kidney function was impaired. Potassium tended to be decreased, but Austin and Berry found 4 of 44 cases with hyperkalemia, all of whom died. The hyperkalemia may have been caused by intravascular hemolysis of red blood cells and widespread tissue destruction. Blood chlorides were very variable with a range of 90 to 138 mEq/l in 47 determinations. Sodium and CO<sub>2</sub> combining power also showed wide variations; the former 124 to 171 mEq/l in 43 patients, the latter 11 to 34 mEq/l in 38 determinations.

Liver function tests may show parenchymal damage. The cerebral spinal fluid may occasionally show elevated pressure and protein values. The urine not infrequently showed albuminuria, red blood cells, white blood cells and hyaline-granular casts. Electroencephalographic and electrocardiographic studies revealed nonspecific brain and myocardial damage which are usually temporary in survivors.

### Pathology of Heat Stroke

Heat stroke affects both the central nervous system and the viscera.<sup>1</sup> The central nervous system showed a progressive destruction of neurons and a proliferation of glial elements. These changes were most marked in the cerebellum, cerebral cortex, and basal ganglia, but not in the hypothalamus or the rest of the brain stem. Malamud, Haymaker, and Custer<sup>2</sup> believed that the cellular changes were the direct effect of hyperthermia. They noted that the degree of cellular pathology corresponded with the duration of survival after the onset of hyperthermia, not to the length of illness in those cases where elevated temperatures were a terminal event. There was also edema, congestion and petechial hemorrhage, most commonly about the third ventricle, aqueduct and fourth ventricle. Malamud, Haymaker, and Custer<sup>2</sup> were of the opinion that these changes were secondary to shock. They observed a direct relationship between the severity of shock and the degree of hemorrhage. Furthermore, the distributional pattern of hemorrhage was analogous to that occurring in diseases associated with shock, but not hyperthermia. The coagulation defects of heat stroke also contributed to the hemorrhage.

The abdominal and thoracic viscera showed both hemorrhage and parenchymal damage.<sup>1</sup> The longer the survival, the more widely disseminated the hemorrhage. No correlation could be made between blood pressure levels and the degree of hemorrhage. Coagulation defects undoubtedly contributed to the hemorrhage. The structures most commonly involved were the lungs, epicardium and endocardium, peritoneum, gastrointestinal tract, pleura, skin, and heart muscle.

The longer the survival, the more severe the parenchymal lesions. Structures involved in order of frequency<sup>1</sup> were megakaryocytes, heart muscle, lungs, kidney, liver, and adrenal cortex. The involvements accounted for the clotting defects, FKG changes, lobular pneumonia, lower nephron nephrosis, and jaundice, sometimes accompanying heat stroke.

### TREATMENT

It is universally agreed that reduction of body temperature as rapidly and safely as possible is needed to reverse the manifestations of heat stroke. Evaporative cooling has been recommended as the best means.<sup>3</sup> After the patient had been wrapped in a wet sheet, several electric fans were directed at him while his skin was massaged through the wet sheet. The purpose of the massage was to aid the circulation through the constricted peripheral vessels. The therapy was said to be preferable to the ice bath because the evaporative effect of one gram of water removed seven times as much heat as the melting of one gram of ice. Also, the ice bath was said to cause cutaneous vasoconstriction thereby interfering with heat loss.

Despite these objections the ice bath has been found to be more effective than evaporative cooling. Daily and Harrison<sup>2</sup> compared evaporative cooling and ice bath treatment on experimentally induced heat stroke in mice. They found more survivors in the ice bath treated group. In 25 cases of heat stroke Ferris and others were able to effect a temperature reduction to 102 F in 9 to 40 minutes by means of the ice bath.

After immersion in ice water a dramatic change in clinical appearance may occur with falling temperature. Abnormal blood pressure may approach normal levels without intravenous therapy. Patients who were unconscious and flaccid may become rigid and delirious. Considerable effort may be required to prevent the patient from escaping the tub or injuring himself. Some may require restraint for several hours after cooling.<sup>3</sup>

It is advisable to cool the patient to no lower than 101 F to 102 F. In one patient treated by ice bath body temperature dropped to 99 F before removal from the ice water. His temperature subsequently fell to 96 F and the patient died in shock.

Shock must also be treated. The vascular collapse is primarily peripheral but cardiac failure may be present in elderly patients. One can treat these by the usual methods of intravenous fluids. Levophed and digitalis. Levophed should be avoided during hyperthermic periods as it interferes with heat loss by inducing peripheral vasoconstriction. Oxygen therapy is probably valuable when peripheral failure, pulmonary edema or cyanosis are present. Wright, Reppert and Cutting recommended vitamin K and early blood transfusions in view of the tendency to hemorrhage. Serious blood loss however is rarely a problem in heat stroke. It is not uncommon that bronchopneumonia complicates heat stroke. Prophylactic antibiotics are therefore in order.

After the emergency state has passed the patient's temperature must be watched because of possible rebound to hyperthermic levels.

The efficacy of adrenal cortical hormones in control of hyperpyrexia has not been definitely demonstrated. Adrenal hormones do have an antipyretic effect and have been used therapeutically to reduce the pyrexia of various infectious diseases. It has been suggested that adrenal cortical hormones act centrally through the hypothalamus. Furthermore adrenal cortical damage can occur in heat stroke. Ingraham, Watson and McLaurin were able to prevent postoperative hyperthermia in 6 patients receiving cortisone after surgery for craniopharyngioma. Hypothalamic damage often occurs during this type of surgery. Waugh attempted to determine if cortisone would show an antipyretic effect in heat stroke. He found that orally administered cortisone in one case and parenteral cortisone in another were without effect on either the hyperpyrexia or anhidrosis of heat stroke. Austin

and Berry<sup>4</sup> gave cortisone to 6 severe cases, but were unable to come to any definite conclusions

### SUMMARY

1 Heat casualties can significantly reduce the strength of a military unit

2 Heat stroke occurs largely in basic trainees transferred from their homes in northern states to southern training camps

3 An acquired or congenital impairment of heat loss may predispose one to heat stroke. Some of these possibilities are discussed

4 Heat illness results from a disparity between heat gain and heat loss of the body

5 Heat stroke is initiated by an excessive heat load which fatigues the hypothalamic heat dissipating center. Impairment of heat loss and a serious rise in body temperature follow

6 The excessive body heat probably damages tissue cells by its action on cell lipids

7 The main clinical findings are hyperthermia, absence of sweat, neurologic signs, and shock

8 Heat stroke affects both the central nervous system and the abdominal and thoracic viscera. The cerebellum displays the greatest damage in the central nervous system

9 The degree and duration of hyperthermia and shock are the principal prognostic signs of heat stroke

10 Laboratory findings are generally non specific. Low platelet counts occur early because of heat damage of megakaryocytes

11 Treatment consists principally of temperature reductions and control of shock. The efficacy of adrenal hormones has not been demonstrated

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# EXTRACORPOREAL CIRCULATION FOR OPEN HEART SURGERY IN A NAVAL HOSPITAL

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THE institution of a program for open heart surgery has engendered teamwork and a great deal of effort on the part of many members of the group. The program started three years before it was employed in the first clinical case here with the experimental use of various types of pumps and oxygenators. This phase of the work was carried out in several animal laboratories in civilian institutions until the past year, when our own surgical research laboratory was commissioned. We believed that we should not use the technic of extracorporeal circulation on a patient until we could repeatedly use it successfully in dogs.

A cardiopulmonary function laboratory, with the availability of cardiac catheterization is a prerequisite. The institution of such a laboratory is the first step in this program, and we were fortunate inasmuch as such a laboratory has been functioning in this hospital for the past 10 years.

The oxygenator we are currently using (fig 1) is of the rotating disk type developed by Dennis and associates.<sup>1</sup> It consists of from four to ten 18 by 18 mesh stainless steel screen disks that are 47.5 cm in diameter. These disks are rotated at 24 r p m within a steel tank to which 4 to 10 liters of oxygen per minute are added.

The oxygen is heated to 39 to 40°C to minimize heat loss in the machine. Each disk will completely saturate 400 ml of blood



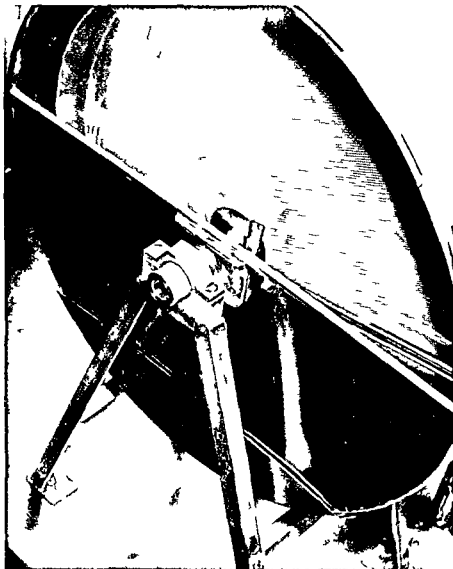


Fig 1 Oxygenator at the center of the disk distributor. The blood on the disk is oxygenated. The low flow rate on the disk is the oxygenated blood.

per minute giving a total capacity of 4 000 ml per minute when 10 screens are used

The blood drains by gravity from each vena cava directly through a distributor to the center of each disk. The blood films out over the rotating disks and the oxygen and carbon dioxide exchange takes place. The saturated blood then drops to the bottom of the tank. The inside of the tank is lightly coated with a silicone antifoam. From the tank the blood passes into the reservoir and then into the pump.

All of the connecting tubing and the reservoir are made of polyvinyl plastic, and the pump tubing is made of gum rubber. The connectors, which are made of very carefully polished stainless steel, are designed to give minimal turbulence. No filter is used with this system. The materials used for the construction of the machine were so selected that it could be sterilized by autoclaving.

The pump (fig. 2) that is utilized in our apparatus is of the multiple finger cam actuated type.\* This is a completely occlusive pump which is simple and reliable. With this type of pump, the flow rate is calibrated before the perfusion is started and then does not change with changes in the patient's blood pressure.

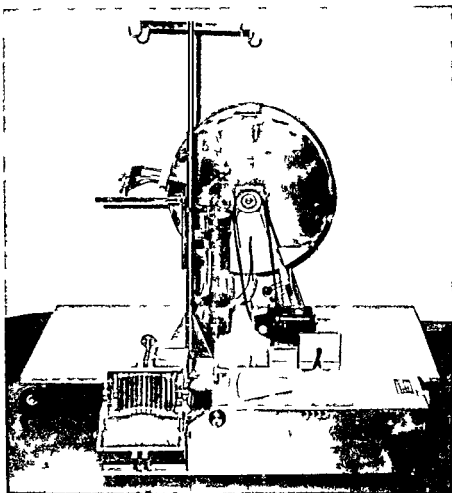
For the anesthesiologist, there are essentially two problems that are created during perfusion. First, there is a loss of anesthetic control because the anesthetic agents are diluted by the blood in the pump oxygenator. Secondly, cerebral hypoxia may develop during perfusion. It therefore is important to guard against drug depression, which will aggravate the hypoxic cerebral depression. Because of the above mentioned problems, anesthesia should be light. The relaxant drugs can be used to control the patient's movements without excessive use of depressant drugs.

When we were satisfied with the technic of perfusion and were confident that we as a team, could use it successfully, the procedure was carried out in our first clinical case on 21 May 1958.

### CASE REPORT

A 6-year-old girl gave a history of frequent colds, a tendency to tire easily, and difficulty in keeping up with her playmates. No history of squatting was elicited, nor were there any episodes of cyanosis, syncope, or convulsions.

Physical examination revealed a girl who was small for her age. Blood pressure in the right arm was 112/70 mm Hg, that in the left arm 114/70, and in the left thigh 120/80 mm Hg. Abnormal physical findings were limited to the cardiac examination. The cardiac apex was 15 cm lateral to the mid clavicular line in the fifth left intercostal space. A prominent systolic thrill was felt over the entire precordial area and was most marked at the left sternal border in the third intercostal space. A harsh grade 3 systolic murmur was heard over the entire precordium but was loudest in the second left intercostal space at the sternal border. The second pulmonic sound was louder than the second aortic sound, and both were clearly defined. The rhythm was regular. Radial and femoral pulses were readily palpable.



Figur 2 P mp a d oxyg i Th TM 2 S gm m t f g p mp th  
f gr d Th xyg tor th f ur cr m d l u th 1 600 ml p  
m i p ty Th pla t ervo al o er a a b b l t ap

The electrocardiogram showed evidence of right ventricular hypertrophy clockwise rotation and incomplete right bundle branch block. A diastolic overload pattern also was present. Roentgenograms of the chest showed cardiac enlargement and plethoric lung fields. Angiocardiography further defined the cardiomegaly by showing an enlarged right atrium and ventricle with a normal sized left atrium and ventricle. Late reopacification of the pulmonary artery occurred indicating a left to right shunt. The mean pressure in the right atrium was 10 mm Hg. Pressure in the right ventricle was 43/6 and in the pulmonary artery 30/9. The mean wedge pulmonary artery pressure was 7 mm Hg. Oxygen saturation studies indicated the presence of a large left to right shunt at the atrial level.

The preoperative laboratory studies revealed essentially normal blood counts and urinalysis. Bleeding time, clotting time, prothrombin time, platelet count, erythrocyte fragility studies, and blood fibrinogen level were normal.

At 0630 on the morning of the operation 22 donors from Fort Totten reported to the blood bank. These soldiers had previously been examined and screened and their blood typed and cross matched with the recipient's blood. Some of the blood drawn was collected in standard ACD solution and the remainder in siliconized bottles that contained 20 mg of heparin in 25 ml of saline solution to 475 ml of blood. This blood was immediately sent to the operating room where it was placed in a water bath at 37°C.

The child was anesthetized with open drop fluothane (brand of trifluoro chlorobromoethane) followed by endotracheal intubation which was aided by Cyclaine Hydrochloride (brand of hexylcaine hydrochloride) spray of the larynx. With the patient asleep a polyethylene tube was placed in a saphenous vein for clasis and for the recording of venous pressure. Both femoral arteries were exposed. One received a plastic catheter for the continuous recording of direct arterial pressures. The other received the arterial cannula from the pump. The latter catheter was not inserted until the patient had been heparinized.

The chest was opened with a transverse anterior incision going through the third interspace on the left side and the fourth interspace on the right with transverse division of the sternum. The thymus gland was dissected from the pericardium which then was opened widely with a T shaped incision. T-will tapes were placed about each vena cava intrapericardially in preparation for inflow occlusion. The atrium was explored through the right auricular appendage and a large secundum type of defect was revealed. The mitral valve which could be easily felt through the defect was essentially normal as was the tricuspid valve. The pulmonary venous drainage was all into the left atrium.

After 27 mg of heparin (15 mg per kilo) was injected into the atrium two No. 22 Bardex catheters were inserted in the atrium and secured with purse-string sutures. These catheters were manipulated into each vena cava and when the cannulae were secured by the tapes the pump oxygenator was started. As the machine functioned well from the start the atrium was promptly opened with an incision extending from one vena cava to the other without actually opening the vein walls.

The defect which measured about 5 by 2 cm and was immediately adjacent to the coronary sinus and the Thebesian veins was closed with a combination of continuous and interrupted silk sutures size 00 and 000. When the defect was closed and it was ascertained that the coronary sinus had not been compromised the atrial wall was closed with a single continuous suture. The tapes about the cannulae were released and the perfusion stopped after 23 minutes. When the

cannulae were removed 54 mg of protamine sulfate (3 mg per kilo) was administered slowly

Blood samples were obtained prior to the actual perfusion at 10 minute intervals during the perfusion and at its termination These were examined for plasma hemoglobin whole blood hemoglobin cell morphology hematocrit platelet count red cell fragility fibrinogen concentration protamine activity clot retraction pH and oxygen saturation These results are tabulated in table 1

A remarkable blood homeostasis was maintained during the perfusion the drop in the platelet count did not interfere with an excellent clot retraction which was normal after giving the patient the protamine Protamine titrations by a rough qualitative method gave an excellent end point for blood coagulability of seven minutes after the protamine was administered Morphologic examination of the cellular elements of the blood samples revealed minimal changes In general no major changes were noted in the blood during or after perfusion

For anesthesia the patient was maintained with Pentothal Sodium (brand of thiopental sodium) Demerol Hydrochloride (brand of meperidine hydrochloride) and nitrous oxide Circle absorber semiclosed technique was used to administer the nitrous oxide The Pentothal and Demerol were given intravenously in divided doses A total of 175 mg of Pentothal and 30 mg of Demerol were used All agents were stopped as soon as perfusion started

During perfusion the lungs were kept inflated with a mixture of helium and oxygen Controlled respiration was carried out throughout the entire procedure including the period of perfusion

Electroencephalographic tracings were made throughout the procedure and at no time was the tracing flat This indicated that circulation to the brain was adequate

Arterial pressure as recorded by the direct method, never was less than 100 mm Hg and during most of the perfusion was 120 mm systolic

At the completion of the procedure the heart demonstrated a 2:1 block with a ventricular rate of 40 A silver coated stainless steel wire was sutured into the left ventricular wall then threaded through a polyethylene catheter and brought out through the chest wall A similar wire was sutured into the anterior chest wall These wires were inserted so that they might be connected to an external pacemaker if cardiac arrest occurred or if the ventricular rate became too slow The chest wall was closed after two No. 40 catheters had been placed in each pleural cavity and connected to underwater suction

Upon completion of the operation the patient's temperature was 90 F and the pulse rate was 46 per minute There was a complete heart block with atrioventricular dissociation and idioventricular rhythm The temperature rose gradually to normal with the aid of an electrically heated blanket and as the temperature rose the blood pressure and ventricular rate also increased The patient was taken to the recovery

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room with a blood pressure of 106/60 mm Hg and a ventricular rate of 72 per min. The electrocardiogram then showed nodal rhythm and the patient was breathing well unassisted.

For the first 5 days a medical officer was in continuous attendance at the bedside. The electrocardiogram was constantly monitored with a cardioscope and a pacemaker to be used in the case of cardiac arrest or marked bradycardia was in the room.

During the night following the operation the patient's ventricular rate increased to 110-120 per min. and the blood pressure was maintained at levels of 110/70 to 110/80 mm Hg. She was breathing well and was mentally alert. There were no neurologic deficits. The urinary output was good and the urine was clear. The hematocrit was 38 ml per 100 ml and the hemoglobin was 13.2 grams per 100 ml at 2300 following the operation. A roentgenogram of the chest showed the lungs to be expanded with no abnormal accumulation of fluid in the pleural cavities. There was no oozing from the wounds. The blood pH was normal and the plasma hemoglobin was essentially normal.

On the first postoperative day the two low thoracotomy tubes were removed. The patient's vital signs were within normal limits but it was apparent that she was not effectively raising her bronchial secretions. There were coarse rales bilaterally and the respiratory rate had increased. She was placed in a croupette. Attempts at tracheal aspiration were not effective. Roentgenograms of the chest revealed a right upper lobe atelectasis with some questionable pneumonitis.

On the second postoperative day direct laryngoscopy and tracheal aspiration were carried out and a considerable amount of mucopurulent secretion was removed. Roentgenograms following the tracheal aspirations showed little improvement in the atelectasis and pneumonitis. Later during the day the temperature rose to 102 F and the respiratory rate increased to 40-50 per min. A tracheostomy was performed and a large amount of secretion was removed.

On the third postoperative day the patient's condition had greatly improved. Her respirations had become less laborious and the breath sounds had assumed an almost normal character. Roentgenograms of the chest showed marked improvement of the atelectasis and pneumonitis. The cardiac rate was 115-130 per min. and there was still a nodal rhythm.

By the fourth postoperative day the patient's condition was considered good. Respirations were normal and she was taking fluids orally in adequate amounts. She continued to improve and the following day was out of bed and an electrocardiogram showed a normal sinus rhythm. On the ninth postoperative day the tracheostomy tube was removed. The lungs were clear and the temperature was normal. All of her wounds were healing well and she was ambulatory. The thrill and loud systolic murmur that were present preoperatively were no longer present. There was obvious decrease in the heart size with a regular

sinus rhythm Roentgenograms showed the lungs to be essentially normal

By the twelfth postoperative day all the sutures had been removed and the wounds had healed per primum. The ventricular wire was removed from the heart with no difficulty. The patient was ambulatory asymptomatic and considered to be well. She was discharged to her home on the fifteenth postoperative day.

### SUMMARY

The institution of an extracorporeal program for open heart surgery requires co-ordinated teamwork and a tremendous effort on the part of each member of the team. It also requires intensive laboratory work, inasmuch as the laboratory is called upon to perform time-consuming and difficult procedures. Only after repeated success in the animal laboratory with the entire team employed, and after sufficient confidence has been obtained in the use of the heart lung bypass procedure, can one feel justified in the use of this procedure in clinical cases.

A successful clinical application of extracorporeal circulation and open cardiotomy for the repair of an atrial septal defect is reported.

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# EXCHANGE TRANSFUSION FOR ACUTE POISONING IN CHILDREN

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**E**XCHANGE transfusion in the newborn period to prevent or remove dangerous amounts of circulating indirect bilirubin is a common procedure in pediatric practice. The indications for and the technic of this procedure is well learned in almost every pediatric residency.<sup>1</sup> Dangerous amounts of other circulating substances are encountered with disturbing frequency in older children. Occasionally the amount ingested and the substance cannot immediately be determined; however, the necessity for additional treatment may be recognized. Because dialysis of almost any nature is technically difficult and not available to most hospitals, exchange transfusion has been found to be effective without undue hazards and may be quickly provided in selected cases of poisoning.<sup>2</sup> As a reminder of this useful tool as a possible lifesaving measure, the following three illustrative cases are presented.

## CASE REPORTS

**C**ase 1. This two-year-old white boy was apparently well until 1100 hours on the day of admission when the mother noted he was holding a bottle of Nembutal (brand of pentobarbital sodium) capsules with an estimated 17 to 20 100 mg capsules missing from the bottle. When the capsules could not be located and the patient became very lethargic, he was rushed to the hospital where at 1130 hours he was comatose with markedly depressed respirations and absent lid and corneal reflexes. Immediate stomach lavage was instituted and was continued until 1300 hours.

Because of the patient's failure to respond to painful stimuli, marked depression of respirations, and the probability of having ingested a large amount of the drug, it was decided an exchange transfusion should be done. By 1345 hours the transfusion had been started through a polyethylene catheter placed in the right femoral vein. The exchange was stopped at 1620 hours after 2,290 ml of whole blood had been exchanged. Midway of the procedure the patient responded to painful stimuli, later moved his extremities and toward completion yawned several times. His vital signs re-

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maintained stable and were reported as pulse rate 100 per minute respirations 14 per minute temperature 97.2°F rectally and blood pressure 116/62 mm Hg at completion of the procedure. Infrequent pharyngeal suction was necessary for 2 to 3 hours and respirations gradually increased to 34 per minute. At 1935 hours he was reported to cry and resist restraints. The night was spent in fairly quiet sleep and he seemed normal the following day. On prophylactic penicillin and streptomycin the wound healed rapidly and there were no further complications.

**Case 2** This three year old white girl was apparently well until she came in from play at approximately 1100 hours on the day of admission to the hospital and complained of abdominal pain and promptly vomited orange colored fluid several times. Upon arrival at the hospital her lower legs and feet were stained a brownish orange by vomitus but otherwise there were no abnormal findings. Stomach lavage was started immediately and continued for 45 minutes when the return had almost cleared. It was noted at 1230 hours that her lips appeared slightly cyanotic however this was at first thought due to the child's crying and resisting lavage. The mother had been sent home to seek out the possible ingesta. She returned with an empty Pyridium (brand of phenylazo-diamino pyridine hydrochloride) bottle which was found beside a garbage can in the neighbor's yard. The neighbor admitted discarding a bottle of Pyridium containing all of the prescribed amount for a kidney infection which she had not used.

On completion of lavage the patient was noted to be quite lethargic. Lethargy and cyanosis became progressively more marked without improvement with oxygen therapy. Venous blood appeared extremely dark and failed to change color on shaking in test tube or on standing. Methemoglobinemia was an obvious diagnosis. A catheterized urine specimen had the appearance of a concentrated solution of iodine. The child's appearance and reaction seemed to warrant immediate further treatment to prevent possible serious sequelae. Intravenous methylene blue was not available. Exchange transfusion was recommended and was started at 1445 hours. After 1400 ml had been exchanged the patient's skin, lips and nail beds gradually became a normal pink color. She tolerated exchange of 2000 ml blood well and on prophylactic penicillin and streptomycin was asymptomatic the following day. Chemical analysis for methemoglobin on pre-exchange blood done two days post exchange revealed methemoglobin 40 grams per 100 ml.

**Case 3** This 28 month old girl was brought to the hospital with a history of ingestion of a minimum of 48  $1\frac{1}{4}$  grain aspirin tablets and an undetermined number of 5 grain tablets approximately one half hour previously. She was immediately given gastric lavage following which the mother thought the child was rather depressed. On admission there was no other abnormal observation made. A blood salicylate level was reported as 73 mg per cent two and one half hours after

ingestion and at four and six hours after ingestion as 121 mg per cent and 160 mg per cent respectively. The blood CO was reported 10 mEq and the attending physician believed there had been progressive signs of intoxication although her temperature remained normal. Appropriate fluids were started intravenously and the patient had voided five times however she also vomited. Eight hours after the ingestion exchange transfusion was decided upon and was completed by 12 hours after ingestion with 1 000 ml whole blood being exchanged. The blood salicylate level was reported as 24.3 mg per cent immediately post exchange. The procedure was well tolerated and her convalescence was uneventful.

### DISCUSSION

During 1956 and 1957 acute poisoning in children was responsible for 142 admissions to Tripler U S Army Hospital, or 2.6 per cent of the total children admitted for all causes. This increased incidence over the usual expected rate of approximately 1 per cent probably is explained by the increased exposure of children living in temporary circumstances to poisons of various kinds and in weather permitting year round outdoor play. There were no deaths as a result of poisoning during the period of study and exchange transfusion was not considered necessary in other children. However subsequent to the period of study there has been one death caused by ferrous sulfate poisoning in which exchange transfusion was considered indicated but the child expired before the treatment could be started.

In order for exchange transfusion to be most effective it should be started at the earliest time possible after evaluation of the patient and the circumstances surrounding ingestion of poison permits. Procrastination may result in irreparable damage to vital organs. However it should be realized that exchange transfusion will be indicated in only a small per cent of patients admitted for acute poisoning.

To facilitate the exchange we have asked the surgical department to place the polyethylene catheter in a saphenous vein through a femoral cut down. The usual precautions should be taken as in transfusion during the newborn period and at least the estimated blood volume of the patient exchanged. Prophylactic penicillin and streptomycin post exchange is an additional routine measure.

### SUMMARY

Acute poisoning in service children appears to be at least  $2\frac{1}{2}$  times a more common cause for hospitalization in Hawaii than generally expected. A small per cent of admissions had ingested and absorbed sufficient quantities to require more than the usual preventive and supportive treatment. Three of 14?

children admitted to Tripler Army Hospital in 1956 and 1957 were treated with exchange transfusion following injection and poisoning with large amounts of either Nembutal (brand of pentobarbital sodium), Pyridium (brand of phenylazo diamino pyridine hydrochloride) or aspirin. No deaths occurred in this period. Exchange transfusion in selected cases of acute poisoning is effective, and without serious hazards when the technic learned by pediatricians for use in the neonate is practiced, and should be remembered as probably the tool of choice when dialysis is needed.

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### MORE DOCTORS—LESS DISEASE?

We are continually being reminded of the advances and progress of medicine and unquestionably many things are possible today which were impossible one or two generations ago. But without detracting from these diagnostic and therapeutic achievements I think it fair to point out that the real progress is much less than is claimed. We have managed to change the pattern of disease that is all. As in everything else, solving one problem leads to the appearance of new ones, often more difficult or intractable than the first, and in some directions at least we seem to be approaching problems that cannot be solved. Proportionately more doctors are kept busy today than fifty or a hundred years ago, but taken as a whole there seems to be no evidence that there is less disease. Where once a man's first illness might well be his last, today he can clear many obstacles before reaching his grave.

—R L MANNING

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# PULMONARY VASCULAR CHANGES WITH STENOSIS OF PULMONARY AND TRICUSPID VALVES AND SMALL RIGHT VENTRICLE

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THE possibility of surgical intervention to alter the natural history of some patients with congenital heart disease has stimulated a considerable amount of interest in clinical diagnosis and also in the pathologic changes that occur elsewhere in the body and are directly associated with the cardiac defect. Nature often performs experiments for us that we may utilize as an investigative tool to further our knowledge of some aspects of medicine. For this reason we wish to report an unusual cardiac defect and the pulmonary vascular changes that occurred with it.

## REVIEW OF LITERATURE

The arterial vasculature of the lung has been arbitrarily divided into elastic arteries, muscular arteries, and arterioles.<sup>1</sup> The structural changes occurring in these vessels after birth were clearly described by Civin and Edwards as follows:

**Elastic arteries.** At birth these vessels are patent oval structures lined by endothelium immediately applied to a wavy internal elastic lamina. This lamina is surrounded by circularly oriented smooth muscle, the external third of which contains scattered elastic fibers. The adventitial portion of the vessel blends with the relatively acellular peribronchial collagenous connective tissue. At birth and shortly thereafter the luminal diameter is equal to or less than the wall thickness. By the first month of life the luminal diameter exceeds the thickness of its wall; the internal elastica becomes heavier; the inner two thirds of the media is constituted by a mixture of collagenous tissue and smooth muscle, and the outer third demonstrates heavier and more numerous elastic fibers. At six months the vessels resemble the adult structure, particularly with equal distribution of elastic fibers throughout the media, and there is no progressive change in size from one to 20 years.

**Muscular arteries** Prenatally these arteries are represented by circular vessels with very narrow lumens, often with cuboidal endothelial cells lying on a thick muscular media surrounded by a collagenous adventitia that merges with the collagenous structures of the surrounding alveoli. Within the first six months the vessel and its lumen increase in size; the wall does not increase as rapidly as the lumen it surrounds, however, so that at six months the latter is larger than the wall. An internal elastic lamina begins to appear between the fourth and the sixth month but not before the fourth month. It is initially represented by discontinuous strands of elastic fiber that fuse and form a continuous membrane, and the adventitia becomes thinner. Growth is the prominent feature from then to one year. There is the development of an external elastic lamina by two years, and from this time until the age of 20 there is a recapitulation of these changes in other muscular arteries, but past 20 no further differentiation occurs.

**Arterioles** These investigators<sup>1</sup> claim that the arterioles are not identifiable prenatally or at birth. At about one month of age the vessels present as small lumens surrounded by a dense connective tissue layer; the developmental changes thereafter consist of progressive increase in luminal size and the formation of a more elastic wall. The time of formation of the elastic lamina was not ascertained; however it was found to be present by the twentieth year.

The progressive vascular changes occurring with age have been studied by Welch and Kinney,<sup>3</sup> and by Civin and Edwards.<sup>2</sup> A systematic progression was noted. In the young individual without pulmonary vascular disease there is little or no fibrous tissue between the endothelium and the internal elastic lamina; in fact, the latter authors stated that they found no intimal fibrosis in the vessels of individuals up to 10 years of age. With the second decade there was noted asymmetrical intimal involvement principally of the muscular arteries and the arterioles. The third decade carried with it the involvement of the elastic arteries as well. By the fifth decade, there was symmetrical intimal collagenization of the muscular arteries and symmetrical fibrosis of the elastic vessels. Further aging was accompanied by progressively more severe effect on the pulmonary vascular structures with two generalizations: (1) changes appeared more severe in the smaller than in the larger vessels and (2) there was an increase in intimal change and increase in the number of vessels involved with increasing age.

It was also noted that as intimal fibrosis became established, fragmentation of the intimal elastic laminae occurred and the vessel walls showed an increase in the collagenous content with diminution in the elastic and muscular components. Welch and Kinney<sup>3</sup> believed the common factor in the changes that they described was a marked increase in pulmonary blood flow.

Hamilton Woodbury and Woods demonstrated that the fetal right and left ventricle pressures are about equal, and it was shown in addition by Lind and Wegelius<sup>1</sup> that in the human fetus the right ventricle supplies blood to the descending aorta via the ductus arteriosus. Civin and Edwards<sup>2</sup> suggested that the high pulmonary resistance necessary for this to occur might not be attributed to the dynamics of the collapsed lung but seem intrinsic in the pulmonary vasculature and that the narrow state of the muscular arteries may be the significant factor. Consistent with this are the postnatal changes that occur principally the widening of their lumina and the thinning of their walls both of which would lead to a decreased pulmonary resistance to flow.

Edwards and Edwards and Chamberlin<sup>3</sup> furthering this line of reasoning, directed attention to the pulmonary vasculature in governing the clinical course of the congenital cardiacs. Other authors cited by Dammann and Ferencz regard the pulmonary changes that occur with cardiac malformation as a separate anomaly of independent origin. This view is based on the lack of correlation in the pulmonary changes with the size of the cardiac defect. Dammann and Ferencz are currently studying this aspect of the problem to attempt to improve the understanding of these particular changes. Edwards has theorized that the vascular changes associated with cardiac defects are a response a compensatory process to enable the individual to survive and that these changes are progressive and may become deleterious to the patient.

The particular instance in which we are interested is the defect between the ventricles and the great vessels permitting increased blood pressure to act upon the pulmonary vascular bed. Under these circumstances the pressure applied to the pulmonary circuit is a function of the size of the defect. In all cases there must be a pulmonary hypertension throughout the life of the individual. The relative blood flow to the greater and lesser circulations is a function of the resistance to flow offered by each. Although the systemic resistance is relatively static the pulmonary resistance varies during life in accordance with the arterial changes in the lung. It follows that three possible clinical syndromes may occur depending upon the possible changes in the pulmonary arterial system.

*Phase I* Pulmonary vascular evolution follows a relatively normal progression with a fall in pulmonary vascular resistance. This results in larger amounts of blood being directed to the lungs and in order to maintain an adequate systemic flow cardiac output increases. Individuals with this condition often terminate in high output failure.

Microscopically the lungs of an individual dying during phase I show extensive congestion with edema of the alveolar

septums, and presence of fluid and heart failure cells. The larger vessels show evidence of medial hypertrophy, the smaller muscular arteries show medial hypertrophy with minimal rare intimal proliferation. The capillaries are engorged, and in general there are no venous lesions.

*Phase II* The pulmonary vessels remain in the fetal state with thick walls and narrow lumina. In those instances the pulmonary and the systemic resistances may be nearly equal, the patient may manifest few if any signs of cardiac decompensation, and may show little evidence of cardiac disease.

Microscopical examination of the lungs of these individuals fails to demonstrate evidence of failure, but rather the alveoli and capillaries are normal. The small arteries retain their thick walls and narrow lumens, and show increased amounts of muscular and elastic tissue in the walls.

*Phase III* Vascular resistance continues to develop in the pulmonary circuit with the result that more blood is shunted to the systemic circulation. Dyspnea and cyanosis are present, growth and development are retarded because of the partially anoxic state.

The increased vascular resistance is caused by marked medial hypertrophy and intimal proliferation. Both small and large vessels are affected. Some small vessels may appear normal; however, serial sectioning usually demonstrates that they lie beyond a point of nearly complete occlusion.

### CASE REPORT

The patient, a male infant, was the fourth-born of a 26-year old Caucasian mother and a 29-year old Caucasian father. There were three living siblings; no history of familial disease nor are the parents related by blood. The mother's blood group is O Rh positive. Her expected date of confinement was 22 September 1957. The date of delivery was 27 September 1957. Her prenatal course was uneventful and there was no history of infection or irradiation during pregnancy. Labor and delivery were not remarkable. The length of the first stage was 10 hours and sedation included Sodium Amytal, Demerol, Hydrochloride, and Chlorpromazine Hydrochloride. Anesthesia for the delivery stage was administered by local infiltration; the second stage lasting seven minutes.

Immediately after birth the infant was noted to be cyanotic; however, he responded well and the initial cry was vigorous. No resuscitation was considered necessary and only bulb suction of the nasopharynx was instituted. Respirations were established in one minute and were considered normal in five minutes. Oxygen was used in the delivery room for 30 minutes. Physical examination at that time revealed an apparently normal newborn baby. The initial cyanosis was



thought by the attending physician to be the result of amyotal depression. It was decided at this point to place the infant in an Isolette with 35 per cent oxygen. The nursing notes indicated that this treatment improved his color slightly and that he seemed active and alert.

On the first day after birth the infant was removed from the Isolette. Cyanosis was noted to persist and to become worse. Pulse rate at the time was 120. Examination of the lung was not remarkable. A grade III harsh systolic murmur was heard over the lower sternum and P2 was diminished but no hepatosplenomegaly was noted. The attending physician entertained the diagnosis of congenital heart disease. A coentgenogram of the chest was thought to indicate a normal newborn chest.

During the first day of life the pulse rate increased to 134 per minute and respirations to 42 per minute. The cyanosis was persistent but the infant's condition otherwise remained unchanged. By 25 hours after birth he was noted to be retracting; respirations had increased to 50 per minute and there was marked cyanosis on slight exertion. By 36 hours after birth cardiac enlargement was noted; the live edge was 2 cm below the right costal margin and 2 to 3 plus pretibial edema had developed.

It was decided to digitalize the patient after an electrocardiograph was obtained that demonstrated left ventricular hypertrophy. A clinical diagnosis of tricuspid atresia with patent foramen ovale was made. By 50 hours after birth the pulse rate had increased to 160 per minute and respirations to 60 per minute. Cyanosis had increased and the child's condition was considered serious. By 62 hours after birth the cyanosis was marked with crying; respirations were labored at 52 to 60 per minute and the pulse rate persisted at about 160 per minute despite digitalization. Physical examination revealed the lungs to be clear to percussion and auscultation; the heart border extended to the left anterior axillary line; the second pulmonic sound was diminished and the previously mentioned murmur persisted. The live edge had descended to 3 cm below the right costal margin and peripheral edema was still noted. Penicillin and streptomycin were given prophylactically.

The infant's condition deteriorated. Periods of apnea lasting as long as 70 seconds were noted approximately 60 hours after birth. By this time the pulse rate had increased to 184 per minute and respirations to 2 per minute. The infant was cyanotic and breathing irregularly. In the terminal three hours the pulse rate dropped from 180 per minute to 120 per minute. Periods of apnea became longer and Cheyne-Stokes respiration was noted two hours before death. Terminally the child had gasping and markedly cyanotic.

During hospitalization no fever was noted. Birth weight was seven pounds and two ounces and terminal weight was seven pounds. Death occurred 7 hours after birth.

A postmortem examination was performed about 13 hours after death. Significant findings included changes in the heart, lungs, and liver. The lungs filled the pleural cavity and there was no evidence of free fluid, exudate, or hemorrhage. The left lung weighed 22 grams; its surface was smooth and glistening; the parenchyma was light red-purple in color, and the left lower lobe showed a deep red-purple area in the dependent portion. The entire lung was crepitant and floated on water, the cut surface being light red-purple. The vascular structures supplying the lung were in their usual distribution. The right lung weighed 29 grams and was similar in description to the left.

The heart was enlarged, weighed 21 grams, and extended from 0.5 cm to the right of the sternal border to the anterior axillary line on the left. The pericardial cavity contained about 5 ml of deep golden-yellow fluid; the surface of the heart was gray and glistening, through which a deep red-purple parenchyma was noted. The right atrium was tremendously enlarged and dilated. The surface area occupied by the right ventricle was small.

Dissection of the vessels at the base of the heart revealed them to rise from their appropriate cavities. The ductus arteriosus was located approximately 3 cm distal to the aortic ring. The right atrial wall measured 3 mm in width. The foramen ovale was patent between the atrial cavities and measured 1.5 cm in diameter. The tricuspid valve, viewed superiorly, represented an inverted cone. The valve ring at the base of the cone measured 2.5 cm in circumference. At the apex of the cone, the valve orifice was represented by a slit 0.6 cm in length and 0.1 cm in width. The valve leaflets were well formed, and although they were fused along their margins, the line of junction was discernible. The chordae tendineae inserted immediately above the valve edge. The small slit-like aperture described above formed a stenotic point in the circulatory path.

The right ventricle was represented by a small underdeveloped cavity; its wall 0.6 cm in width and its endocardial surfaces smooth, shiny, and translucent. The papillary muscles were large, and the chordae tendineae well formed. The interventricular septum demonstrated no persistent interventricular communication.

There was no evidence of infundibular stenosis. The right ventricular outflow tract was essentially closed by a stenotic pulmonic valve. This structure was represented by a dome-shaped fusion of the valve leaflets. The circumference of the pulmonic valve ring was 1.0 cm. The leaflets were well formed, and the line of fusion between adjacent cusps was evident. The orifice was situated at the highest point of the dome and was a tiny slit-like orifice that would just admit the tip of a needle. Approximately 1 cm above the pulmonic valve ring, the pulmonic artery was circumferentially narrowed so that its lumen had a diameter of about 0.5 cm. The lumen before and after that portion, however, was 1 to 1.2 cm in diameter.

The left atrium was not remarkable except for the patent foramen ovale previously noted. The left ventricular cavity was not remarkable. The left ventricular wall measured 0.9 cm in width. The mitral valve circumference was 4 cm. The aortic valve circumference was 2 cm and the coronary vessels were not remarkable. The ductus arteriosus previously mentioned was 1 cm in length. The venous system of the surface of the heart and the coronary sinus were remarkably dilated.

Careful dissection of the arch of the aorta failed to reveal any further abnormality. The liver was enlarged, weighed 360 grams, extended 2.5 cm below the right costal margin. The capsule was smooth and shiny through which a red purple parenchyma was noted. Aside from passive visceral congestion, the rest of the postmortem examination was not remarkable save for a solitary frontal lobe brain cyst.

Microscopic examination of the liver and kidneys demonstrated congestion, and of the brain demonstrated a cyst, the margins of which failed to show evidence of gliosis or inflammatory infiltrate.

Microscopic examination of the lungs was of particular interest. Many of the alveolar spaces were filled with an eosinophilic granular material containing scattered hemosiderin-laden histiocytes. There were large confluent alveolar spaces, the walls of which were formed by hypercellular septums. There were areas particularly in the upper lobes bilaterally that demonstrated failure of expansion; in these areas the alveolar walls were collapsed and adjacent. In other areas the alveolar septums themselves were edematous. The alveolar capillaries were markedly distended with blood.

The bronchial and bronchiolar structures of the lung were not remarkable, but the pulmonary vascular tree demonstrated changes we would like to describe in detail. In examination of the lung tissue making use of the routine hematoxylin and eosin stain and also Verhoeff van Gieson's and Gallego elastic tissue stains, we observed the following:

*Elastic arteries.* The larger elastic arteries accompanying the primary bronchial division were in general lumenally as wide as the air passages they accompanied. The adventitial portion was composed of collagenous connective tissue. The media was formed of elastic and muscular tissue; the elastic fibers were nearly evenly distributed throughout the medial portion and were well formed. The internal elastic lamina was a prominent, rather smooth instead of wavy structure. We also were able to demonstrate areas of fragmentation of this structure. There were asymmetrically placed areas of intimal fibrosis (fig. 1) lying above the internal elastic membrane and often above the areas of fragmentation (fig. 2). The endothelium was represented by a thin line of flattened cells.

In the small elastic arteries the over-all diameters were still equal to the air passages they lay near. The intimal and medial changes



Figure 1 Photomicrograph of an elastic artery showing a plaque of intimal fibrosis with fragmentation of the internal elastic lamina (van Gieson's elastic tissue stain  $\times 440$ )

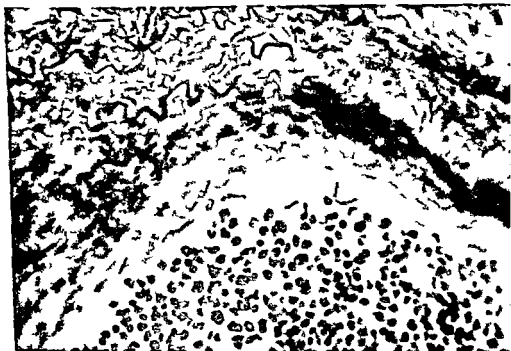


Fig. 2 Photomicrograph of an elastic artery showing fragmentation of the internal elastic lamina (van Gieson's elastic tissue stain  $\times 440$ )

nored in the larger vessels were present in these structures also but more infrequently. These vessels demonstrated a cuboidal endothelium lying upon a wavy internal elastic lamina with a predominance of elastic tissue fibers in the outer third of the media. Even in these structures however the media was thicker than one would anticipate and the lumen larger (figs 3-4).

*Muscular arteries* The muscular arteries were circular in cross section and in general their luminal diameter exceeded the thickness of the wall including the intima, media and adventitia (fig 5). Often the lumen exceeded twice the thickness of the wall. The intimal lining varied from a cuboidal to a flattened cellular structure lying upon a heavy muscular media. In about 20 per cent of these vessels a ring formation of an internal elastic lamina could be demonstrated by Gallegos stain. (We were unable to demonstrate this photographically on black and white film because of the hue differences in blue and purple.) In general the luminal diameter of these vessels was less than that of the nearest bronchiole. In H and E stained sections an eosinophilic smudging was noted along the intimal linings.

*Arterioles* Arterioles were identified by the adventitial collagenous connective tissue that surrounded the small lumen. The wall was virtually no muscular or elastic tissue within their walls. These vessels were patent and their luminal diameters were less than the wall width (fig 6).

## DISCUSSION

The mechanism of formation of this or any particular congenital defect is not known. However the general association of right ventricular under-development, tricuspid valve anomaly and pulmonic valve failure of development is a commonly occurring triad. The particular instance that we are reporting included right ventricular under-development, tricuspid stenosis with but a minute orifice, pinpoint valvular pulmonic stenosis, widely patent foramen ovale, patent ductus arteriosus and a well-developed pulmonic artery with an area of post-valvular stenosis presenting a demarcated circumferential narrowing a short distance from the stenotic pulmonic valve. It is interesting to note that the diameter of the interauricular communication was greater than that of the pulmonary artery at its widest point 1.0 cm, and of the aorta at its origin 0.7 to 0.8 cm.

It would seem that the prenatal circulation was as follows. Blood returned via the vena cavae entered the right auricle and passed via the foramen ovale to the left auricle thence to the left ventricle and to the aorta. Considering the stenotic pulmonic valve, the tricuspid stenosis and the under-developed right ventricle, little blood flow would be supplied via this route to the pulmonary bed. In fact the widely dilated ductus arteriosus would expose the pulmonary vasculature to systemic pressure. In other words the systemic and pulmonary circuits were supplied



Figure 3 Photomicrograph of an elastic artery well formed, but with increased amount of elastic tissue (Van Gieson's elastic tissue stain  $\times 440$ )



Figure 4. Photomicrograph of same field as in Figure 3 ( $\times 400$ )

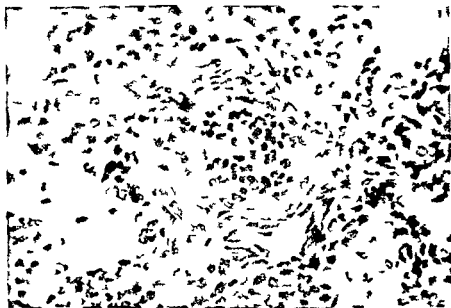


Fig. 5. Photomicrograph of a medium-sized artery showing a highly cellular wall (G. L. L. t. d. m. ter. f. u. h. b. x. c. d. d. th. u. a. l. l. u. d. th. (G. L. L. t. t. t. x 400)



Fig. 6. Photomicrograph of a glomerulus showing a dense cluster of cells (G. L. L. t. d. m. ter. f. u. h. b. x. c. d. d. th. u. a. l. l. u. d. th. (G. L. L. t. t. t. x 440)

by a common ejectile force as mentioned by Edwards, Edwards and Chamberlin<sup>6,7</sup> Postnatal circulation was probably identical to prenatal circulation. One can only speculate as to the volume of blood directed to the pulmonary circuit in view of these circumstances.

We believe that this child died in high output cardiac failure in an attempt to compensate for the poor aeration of blood, teleologically speaking. Dammann and Ferencz<sup>8</sup> have postulated three possible courses or clinical syndromes for individuals with this type of cardiac anomaly. They theorize the progressive fall in peripheral vascular resistance in the pulmonary bed, with a larger and larger portion of the cardiac output being directed in this manner. Cardiac output rises in an attempt to compensate for this loss, and high output failure frequently ensues. It seems to us that some features of this infant's condition fitted the picture of phase I, but the pathologic changes of the pulmonary vasculature, notably the elastic arteries, were more marked than those reported.

We call attention to this case because of the rather marked vascular changes, particularly in the larger elastic arteries, which would be exposed to the highest pressure gradient. These, including intimal proliferation and fragmentation of the internal lamina, are considered by many to be early degenerative changes. We find this of decided significance in view of the fact that this patient was only three days old at the time of death. We know of no previous report of so marked vascular change in such a young infant. On the basis of the work done by Civin and Edwards<sup>2</sup> by Dammann and Ferencz,<sup>8</sup> and by Welch and Finney,<sup>9</sup> these vessels demonstrate age changes compatible with six or more months of life.

The apparent rapid "aging" of these vessels raises an interesting point. Fetal ventricular pressures are about equal, but blood flow occurs from the pulmonary artery via the ductus arteriosus to the aorta. This route presupposes a higher pressure at the pulmonary end of the ductus, and therefore in the pulmonary artery than in the aorta at the aperture of the ductus. The best explanation for this phenomenon includes competency of the pulmonic and aortic valves, and high pulmonary resistance—either on the basis of a collapsed lung phenomenon or the intrinsic vascular structure—and a lower systemic pressure. Blood in the pulmonary artery and aorta at the moment of valve closure must be equal; however, the rapid "run off" in the systemic bed would result in the higher pulmonary artery pressure necessary for this to occur. Total systemic pressure is the sum of the right and left ventricular pressures, assuming no obstruction to flow.





Fig 5 Photomicrograph of malarial parasite in liver tissue (Giemsa stain, ×400)



Fig 6 Photomicrograph of glomerular pathology in kidney tissue (H&E stain, ×440)

prosthetic polyvinyl sponge. In most cases this is purely a cosmetic procedure, but it can be attended by the complications of major surgery, in the case of polyvinyl sponge, there may be excess hardening and shrinkage resulting from fibrous invasion of the material.<sup>2</sup> It is understandably not a procedure that is justified in military practice. Occasionally, dermis fat grafts are warranted after simple mastectomy for benign disease. The removal of a breast is a severe emotional handicap to a woman. In some instances it is possible to reconstruct the mammary eminence with local flaps, after removal of all underlying breast tissue in benign lesions.

The other form of mammoplasty is breast reduction for over large, or hypertrophic breasts. In massive mammary hypertrophy or gigantomastia, definite pathology can result.<sup>3</sup> Kyphosis, cervical and dorsal spine arthritis, and grooving of the shoulders, all can result from excessively overweight breasts.<sup>4</sup> This is analogous to a woman carrying a heavy sack of sugar suspended from each shoulder. Under these conditions, a mammary reduction operation is a necessity (fig. 3). Again, each case must be considered on individual merit.

The technic of dermabrasion, or surgical abrasion of the superficial skin layers is widely practiced today. This technic was developed during World War II for removal of imbedded dirt and debris in wounds. It since has been adapted for the ablation or camouflage of acne scars, decorative tattoos, benign lentiginous spots, moles, and other benign skin lesions.<sup>5</sup> It most commonly is sought after by victims of acne-scarring of the face. The operation is simple and merely involves the abrasion of superficial skin by sandpaper wire brushes, or similar devices. Morbidity is low, and mortality negligible. In the military it is indicated for treatment of traumatic tattoos or scars, and to improve healing of wound edges after scar excisions. Acne cases must be carefully selected.

The number of decorative tattoos in military personnel is legion. Tattoos often are acquired while the individual is intoxicated. Self-decoration is thought to be related to "attention getting mechanisms" or possibly the desire for self assertion. Frequently, the young serviceman regrets his action almost immediately. By and large, the removal of tattoos from all those who desire it is impossible: there are not enough beds, operating rooms, surgeons or hours in the working day. It also must be remembered that the removal of a tattoo frequently involves skin grafting, a major operation with the inherent danger of complications such as partial loss of the skin graft and infection. There are certain instances however when it may be considered. A patient who has been tattooed while stuporous, it having been arranged for by well meaning but misled comrades is a candidate for operative removal. Certain religions ban this sort of decoration and in

lord should be made and elective surgery categorized as to priority

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## COURTESY IN THE OPERATING ROOM

Good m n n e r s are i m p o r t a n t e v e r y w h e r e i n t h e h o s p i t a l I n t h e o p e r a t i n g r o o m t h y a r e a n e c e s s i t y T h e r e i s n o p l a c e a n d n o o t h e r t i m e w h e n t h e s u r g i c a l p a t i e n t h a s m o e t t a k e t h n d u r n g t h e r e l t i v l y s h o r t p e r i o d h s p e n d s i n t h e o p e r t i g s u t e T h e e x e r c i s e o f c o r r e c t c o n d c t b y m e d i c l d n u r s i n g p e r s l f a c i l i t a t s g o o d t e a m w o r k a n d o f f s p r o p e r p r t c t o n t o t h e p a t i e t d u r n g t h s e c r i t i c a l m o m e n t s

D s o l a y s o f b a d t m p e i l l b e c o m e a n y p h y i c i a n b u t t h e y e n t i r e l y o u t o f p l a c e i n t h e o p e r t i n g r o o m T e a m w o r k c a n b e d e s t r o y e d b y t o n g u e l a s h i n g s u s e o f i m p r o p r l a n g u a g e t h r o w i n g n s t r u m e n t s c o n t a n t c o m p l i n i n g a n d u n d u e s a r c a s m E x c e s s i v e g o o d h u m o r p a r t i c u l a r l y w h e n c c o m p a n e d b y l o u d l a u g h t e r a n d h o r s e p l a y b r e e d i r r e v e r e n c e a n d r e p t t o l d t o d i s t a c t i o n t i m e w s t n g f o r g e t f u l n e a d p e r h a p s m o e s e r i o u s e r r r

—ALLAN J RYAN M D

C t l S t t M d l J u m l  
p 821 S p t 1957

# THE MANAGEMENT OF LATE PROBLEMS FOLLOWING PEDIATRIC CARDIOVASCULAR SURGERY

BERNARD A. YABLON  
NICHOLAS G. BOTT

WITH advances in the treatment of congenital cardiovascular disease, with these conditions are now far beyond the life expectancy of many of this, however physicians are faced with the late postoperative care of these children.

The purpose of this article is to discuss the problems encountered during the care of these children, some 6,000 miles from the congenital heart surgeon, presenting recurring problems of management of original cardiac defects or as they are created by the surgical procedure. These problems were all different in regard to the management of some of the functional problems and the recognition of the existing functional problems, awareness of impending difficulty, and the anatomy is disrupted by a congenital defect. It seems most important in supporting these children.

## CASE REPORT

**Case 1** This patient was a seven month old who had undergone surgical intervention three and one half months while living. The anterior limb of a double aortic arch was ligated.

She was first seen two days after surgery, had been manifesting symptoms of an upper respiratory infection for the previous two weeks. There was no fever, but there were physical signs and roentgenograms.

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From Ryuky Army Hospital, U.S. Army,  
F. C. I. C. P. Y. B. I. P. T. N. T. D.  
N. Y.

monia at the base of the right lung field. On admission to this hospital a white blood cell count was 11,100 per  $\mu$ l with 27 per cent neutrophils and 69 per cent lymphocytes. Throat culture was negative. An electrocardiogram was within normal limits.

The infant was given 300 mg (300,000 units) of procaine penicillin G intramuscularly each day for five days with complete clearing of the previously described rhonchi in the right lung field. A follow-up roentgenogram of the chest in one week showed complete clearing of the infiltration at the right base. After this episode there was periodic stridor in the recumbent position.

On another occasion the infant developed a streptococcal sore throat and purulent otitis media caused by hemolytic *Micococcus pyogenes* var. *aureus* (*Staphylococcus aureus*) organisms. These conditions responded rapidly and satisfactorily to a 10-day course of procaine penicillin G 300 mg given intramuscularly each day together with Terramycin (brand of oxytetracycline) administered in the form of ear drops. Subsequent fluoroscopic studies with barium by mouth revealed an indentation of the posterior aspect of the esophagus by the posterior arch and a persistent narrowing of the lower trachea. Over a 10-month period there was a gradual diminution in the frequency of stridor. At present growth and development are normal. The parents have been instructed to bring the child to the clinic at the earliest signs of respiratory infection.

C 2 An eight-year-old Caucasian girl was seen in the outpatient department of this hospital on several occasions during the period from November 1956 through March 1957 for frequent upper respiratory infections and one episode of bronchopneumonia.

She had arrived at this command three and one-half years following a right Blalock-Tausig procedure for treatment of Fallot. Because of her small stature, congenital scoliosis, and a wide bridge of the nose, she had also been studied for Bonnevie-Ullrich syndrome of ovariangenesis and congenital anomalies. However, the urinary follicle-stimulating hormone excretion was normal. Previous roentgenograms of the chest had shown increased right pulmonary vascularity.

On 20 March 1957 the child was given a course of penicillin for pharyngotonsillitis. On 26 March 1957 she developed a fever of 102 F, a diffusely erythematous urticarial eruption, and one episode of transitory respiratory distress.

Physical examination revealed slight cyanosis of the lips and nail beds, a diffusely red pharynx, fine moist rales in the right lower lobe posteriorly, and a loud systolic left parasternal murmur, most marked in the fourth left intercostal space, transmitted throughout the precordium. The right radial pulse was not palpable, and no blood pressure could be obtained in the right arm. The blood pressure in the left arm was 80/50 mm Hg. There was marked sinus tachycardia of 160 per minute. The patient was orthopneic and the veins on the dorsum

of her left hand failed to collapse until elevated 20 cm above the level of the atria. Weight was 33 pounds.

At that time the white blood cell count was 17 050 per  $\mu$ l with 83 per cent neutrophils. The hemoglobin was 15 grams per 100 ml. A red blood cell count was 5.1 million per  $\mu$ l. A roentgenogram of the chest revealed only an increased right pulmonary vascularity (fig. 1). An electrocardiogram showed right ventricular preponderance.



*Figure 1 (case 2) Roentgenogram showing increased vascularity of the lung field.*

Because of the persistent tachycardia over a period of one and a half hours and clinical evidence of left ventricular failure, she was digitalized with 0.25 mg of digoxin every 12 hours for four days with a maintenance dose of 0.25 mg each day. The symptoms cleared within 36 hours after admission. On the third hospital day, an additional soft to and fro murmur arising from the mitral valve in the right subclavicular and right interscapular area was heard. She was discharged on the seventh hospital day with a maintenance dose of 0.25 mg each day. During a 10-month follow-up, she had no respiratory infections and has no dyspnea on normal activity.

C 3 A three year old Caucasian boy with symptoms of a respiratory infection was first seen shortly after arrival at this command. At 10 months of age he had undergone surgery at Brooke Army Medical Center where a Blalock procedure for tricuspid atresia was accomplished. Preoperative diagnosis had been established by the presence of cyanosis, electrocardiographic evidence of left ventricular hypertrophy and an angiogram which showed direct passage of the dye from the right to the left atrium. At operation the right subclavian artery was anastomosed to the pulmonary artery just proximal to its bifurcation.

On physical examination the child was mildly tachypneic and cyanosis of the lips and nail beds which increased on crying. A loud systolic murmur was heard best in the third left intercostal space transmitted throughout the left precordium. There was left ventricular enlargement to percussion. The liver edge was sharp and moderately tender on palpation one finger breadth below the right costal margin. A roentgenogram of the chest revealed transverse cardiac enlargement and evidence of bilateral pneumonia (fig. 2). The white blood cells numbered 11,750 per  $\mu$ l with 66 per cent neutrophils.

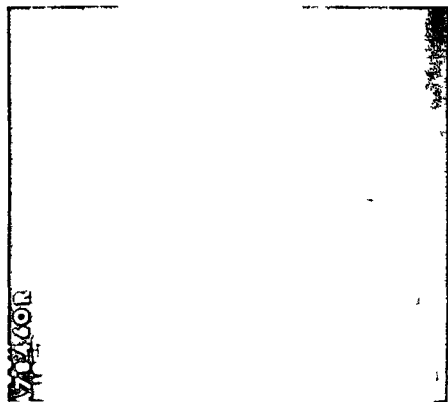


Fig. 2 (3) Evidence of left ventricular enlargement and pneumonia in the right lower lung field.

The patient was treated with Terramycin (brand of oxytetracycline) and on examination four days later the lung fields were clear on percussion and auscultation. The apical rate was down to 80 per minute and the liver was barely palpable at the costal margin descending one fingersbreadth on deep inspiration. Three weeks later an additional soft systolic and diastolic murmur was heard below the right clavicle transmitted to the back just medial to the right scapula. This was thought to arise from the site of the anastomosis. Antibiotics were discontinued at that time without recurrence of original symptoms. Since this episode the patient has been well and is being followed at three-month intervals. He has had occasional slight dyspnea but no orthopnea. He does develop facial cyanosis on crying.

### DISCUSSION

The problems presented here are centered around the management of recurrent respiratory infections and those arising from the altered cardiovascular dynamics created by surgery as well as the primary defect. The good operative result in case 3 most likely depended on the presence of an adequate pre-existing right-to-left shunt at the level of the atria. It is interesting to speculate that in the presence of pneumonia there was a significant increase in pulmonary capillary pressures which were transmitted back through the shunt to the left ventricle, and then back across the atrial defect to account for the apparent increase in systemic venous pressures.

In case 2 the problem was more one of increased left ventricular workload resulting from the surgically caused left to right shunt. This combined with the increased ventricular work from fever led to high output failure. The delayed onset of mild failure is something which one would expect in any large series of postoperative tetralogies. One of the more common patterns described by Gross<sup>1</sup> was the onset of cardiac failure early in postoperative course resulting from the additional burden placed on the left ventricle. It was his experience that if there was no evidence of failure within five or six months, there would be little risk of this later on.

Other possible late complications, including a thrombosis or contracture at the site of the shunt and continuing susceptibility to subacute bacterial endocarditis, should also be kept in mind. Following the ligation of the anterior component of a double aortic arch, Gross noted marked improvement in the tracheal airway but there may be some persisting deformity in the tracheal cartilage as evidenced by intermittent stridor in case 1. There appears to have been some resolution of the tracheal compression in this case however, and there are fewer recurrent infections inasmuch as tracheal development is now proceeding along more physiologic lines.



None of the patients required oxygen for the episodes described above although it was kept in mind for case 2. All were maintained on supplemental vitamins and were seen regularly in the outpatient pediatric clinic.

With regard to the choice of a digitalis preparation digoxin has proved most convenient. For example, in case 2 a digitalizing dose of 0.066 mg per kilogram was used corresponding to the dosage ranges used by Sapin, Donoso, and Blumenthal.<sup>2</sup> Their studies suggested the use of 0.075 mg per kilogram during the first year of life with a maintenance dose of 33 per cent of the digitalizing dose. Slightly lower dosage ranges were used in the older age groups. Another advantage of digoxin is its reasonably rapid onset of action and the several forms in which it is available for clinical use. This includes a liquid preparation with which maintenance dosages can be more easily controlled in small infants.

In transitory heart failure associated with mild respiratory infection a satisfactory response may be obtained in some cases by the use of 0.025 ml of Mercuhydrin (brand of meralluride) per kilogram per day in lieu of digitalization. On the other hand, as illustrated by case 3, the use of cardiac drugs may not be necessary because the treatment of the respiratory infection may result in the rapid resolution of mild heart failure. Not needed in our group but indicated in severe dyspnea is morphine sulfate 1.0 mg per 10 lb body weight.

Much of the cardiac symptomatology between acute episodes has been controlled by the spontaneous limitation of activity by the children themselves.

### SUMMARY

In each of three cases of congenital cardiovascular malformations observed at this hospital there has been an excellent operative result. Some of the problems referable to a combination of the original defect and the altered cardiovascular dynamics which were manifested at various intervals following surgery have been described. The plan of treatment outlined includes early and vigorous therapy of respiratory infections, the judicious use of digitalis, and maintenance of adequate nutrition and general health. The increasing frequency of this type of pediatric patient and the excellent response to standard methods of treatment have been emphasized.

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# CHILD GUIDANCE CLINIC PRINCIPLES AND CRITERIA FOR ESTABLISHMENT AND EVALUATION

FREDERICK A. ZEHRER *Lieutenant Colonel MSC USA*

**I**N THE 10 year period since the establishment of the first child guidance clinic in a military hospital,<sup>1, 2</sup> several similar type units have been organized not only in the United States but also in overseas commands. The intent, undoubtedly, has been to meet effectively the many needs and demands for the specialized services usually provided in a clinic so designated. In terms of the overall mission of the medical services of the Armed Forces there is full justification for the maintenance of child (parent) guidance units.

However, in efforts to serve military parents who have children with problems, or whose unusual adjustment contributes to anxiety in the parents, some practices may well be employed which could do more harm than good. It is an application of the principle "A little knowledge may be a dangerous thing." A recent article<sup>3</sup> in the *U S Armed Forces Medical Journal* serves to underscore the need for caution and sound professional knowledge in setting up a child guidance program, full or "modified."

A working hypothesis that "professional services offered should meet highest possible standards in practice or not be available" should be the guide to any who plan, or have already organized, a child guidance clinic in a military medical installation. Sufficient data and professional opinion in civilian and military settings have been accumulated to serve as guideposts for those interested in extending specialized assistance to parents and children.

It is believed that a presentation of basic working principles and proposed criteria for the establishment and maintenance of a child guidance program in military medical units is needed and can be constructively useful. Prior to listing suggested criteria, a few pragmatic principles are presented for consideration.

## PRAGMATIC PRINCIPLES

The need for child guidance services exists whenever there are more than a few hundred military families for whom medical service is provided on an outpatient basis. Any practicing pediatrician or psychiatrist can supply ready documented opinion on this point.

Once established a clinic has such a heavy demand for services that a backlog soon develops. The largest and best clinics (civilian as well as military) cannot possibly meet all requests for treatment. Therefore a reality principle requires acceptance of this fact and that measures should be taken to control the situation. This can be done by recognizing that *first* priority in time demand must go to active duty military patient needs. Therefore blocking out a child guidance clinic schedule (adapted to local conditions) and holding to it is a necessity. Deviation from this except to deal with a unique situation will only result in a scattering of effort and time taken from other military requirements.

A clinic of this type requires a multi discipline team working in close cooperation. The pediatrician, psychiatrist, neurologist, social worker, and clinical psychologist are key personnel who are needed inasmuch as any situation brought to the clinic involves the family unit (not the child alone). Therefore a basic principle may be stated that effective liaison and communication must be established. This can be done most efficiently through inclusion of such specialists as are needed on the clinic roster (regardless of primary duty designation). Staff personnel of other services for children should be invited and encouraged to participate in case conference sessions *e g* in a general hospital physical medicine, dermatology, and ENT. Frequently psychosomatic and primarily organic symptoms as occur in cerebral palsy and postpolio conditions present problems of a mental hygiene nature where guidance may assist in obviating or relieving emotional problems.

Inasmuch as a child's primary occupation is that of a pupil it is essential that effective communication be maintained with the schools in the area. A guiding concept of a well operated clinic includes this action as a standing operating procedure. In view of his training this liaison function is best delegated to the staff social worker. As in any good communication there is a mutual exchange of pertinent information concerning the welfare of the child but without medical personnel violating personal family data which should be kept strictly confidential.

Another principle too often not observed is that the referring physician should receive a report (if on the local staff he should be invited to participate in the professional staff diagnostic

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discussion) of the clinic appraisal of the family situation. If treatment is indicated, he should be given the opportunity to continue with the treatment or request the clinic (or other unit) to carry on. Too frequently, a patient referred for consultation becomes the "property of the clinic," without the concurrence of the doctor who initiated the consultation referral.

Another principle is that the child guidance clinic should not provide services needed by patients that are available to them elsewhere. For example, if a school in which a patient is enrolled provides speech correction or remedial reading, or both, the clinic should not take over this function, although the staff may be equipped to offer these services.

Medical records on patients examined or treated in the clinic should be kept on file for at least six years and not disposed of as are other records. The regulations on convenience files and for "research and training purposes" permits this to be done. Because of the nature of the problems usually treated in such a clinic, there is often need for future reference to these charts.\*

It is vital that there be recognized the concept that there are no short cuts in the treatment of problem situations seen in a child guidance clinic. Scanning examinations, words of advice, simplification of diagnostic study because of "expediency demands," "sending parents home to carry out suggestions," et cetera, are not present in a competently operated clinic.

Subsequent to direct diagnostic evaluation and staff discussion, resulting in at least tentative diagnostic and prognostic opinions, it is essential that the parents be seen for at least one interpretive type session, even if it is to be the terminal one—e.g., in the event that treatment by the clinic is not feasible or possible, or, where treatment is not indicated. The operating procedure should ensure that this is done by the designated staff member. The same person should be certain to forward a clinic report to the referring physician.

All children seen in a child guidance clinic should have a physical examination, preferably by a pediatrician. The findings should be available to the psychiatrist when the child is first seen. As a working principle, it is desirable to request parents to have this done if the case was not referred initially by a pediatrician when informing them of the date of the initial clinic appointment. The parent can be requested to have such a physical examination done in the medical unit which serves the family's location, and to ask the physician to forward a copy of his findings directly to the clinic. The child's health record also should be brought in (as to any other clinic). Observance of this principle

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is not only an economy measure but prevents overlooking essential medical data

When a parent requests the clinic's service on the advice of the school principal or guidance counselor the parent can be requested (in initial conversation) to ask the school principal to forward a brief report to the clinic. It has been found to be most practicable to be specific in requesting such reports. As a minimum the following should be included: (a) scores on any standard tests administered to the child; (b) teacher rating of the child on such items as acceptance by classmates, special interests and abilities, special disabilities or handicaps, social adjustment in school, level of academic work in terms of grade expectancy; and (c) any data pertinent as to why the child was recommended to be seen at the clinic. A mimeographed sheet of paper with the aforementioned outline can be given the parent to assist in the accurate transmittal of the request (address of the clinic should be included).

It is an important working concept that both parents be seen together at the clinic at least in the initial history phase of the evaluative procedure. Of course, if the father is away on extended TDY, or at an overseas station this is not possible. Because it is a family matter it is only proper that both parents be treated with equal respect and also to determine relative degrees of awareness of a problem. Certainly such a session reveals much to the examiner concerning relative parental roles and intercommunication.

Staff conferences should be scheduled as regularly as are the clinic appointments. It is absolutely essential that the various examination findings and impressions be pooled and mutually evaluated to arrive at a definitive albeit tentative diagnostic opinion plus an estimate as to the need for treatment, if any. In a well run child guidance clinic this many discipline coordination around one table provides not only excellent cross training for personnel participating but a more sound professional opinion than one made unilaterally. As necessary as is such a staff session for initial evaluation, so is also a staff review after therapy has been under way for a few weeks or months. In any hospital which provides residency training in psychiatry, neurology and pediatrics as well as internship training in clinical psychology and field work in social work the establishment of such a clinic is essential to provide proper training to meet diplomate requirements.

The foregoing principles epitomize some key points of a practical nature. They are not all inclusive but serve to delineate the responsibilities involved when specialized mental health services are offered to patients.

With this preface on principles the following proposed criteria for a child guidance clinic are presented. They could be used by a visiting officer as a guide.

## CRITERIA

1 The designated clinic should include on its basic staff at least one qualified psychiatrist, a social worker, and a clinical psychologist. Each of these should have prior training and experience in child guidance procedures.

2 There should be available in the same medical unit (or in one close by) a qualified pediatrician and neurologist. It is desirable that other medical personnel be present in the hospital, to whom referral may be made for specialized evaluation when needed.

3 The clinic should be established in a setting where military patients are not seen at the same time. (For example, a mental hygiene clinic located in a troop training area is not desirable. Instead, the clinic should be held in the hospital or post dispensary area.)

4 The clinic should have a room set up as a play diagnostic and therapy room, with proper equipment available for diagnostic and therapeutic purposes.

5 The waiting room should be equipped with some items geared to children's level. These can be removed on the days when the child guidance clinic is not in session.

6 The clinic should be operated at a designated time, and patients seen only on an appointment basis. In a military setting, such a clinic should have a minimum of four hours, and a maximum of eight hours weekly for patient appointment time.

7 The clinic should schedule a period of at least two hours weekly for case conference discussion purposes.

8 The case conference discussion group should be composed of assigned personnel (who see patients in the child guidance clinic) as well as neurologists and pediatricians. Residents and interns should be invited to sit in on such conferences.

9 The scheduling of "new" patients should be done only for one half of the clinic appointment time. The other half should be devoted to treatment time.

10 When a child is in therapy, the parents (or one parent, in an unusual case) are treated concurrently by another staff member.

11 If a child patient under treatment is enrolled in a school, liaison should be maintained with the proper school personnel when this is indicated (in most instances it is).

12 An effective record book (log book) plus a numerical file and record system should be maintained at all times, separate from other (e.g., adult outpatient) clinic records.

13 Treatment note records should be kept current by the personnel who treat patients in the clinic. Any staff conference

notes correspondence notes on forwarding of reports, et cetera should be kept in the patient's folder. The file should be maintained in a location readily accessible to the staff.

14 If there is a resident in pediatrics on the hospital staff he should be assigned to the clinic for a three to six month period as a staff member. Second or third year residents in psychiatry should be assigned a minimum of a total of six months during their last two years. If a clinical psychology intern is assigned to the hospital he should be on duty in the clinic for a three month period.

15 Effective liaison should be maintained with all other clinics in the hospital which include treatment of children in their specialties.

16 Provision should be made for proper supervision of personnel assigned to the clinic in training status.

17 Treatment should be conducted by various staff personnel within the range of their known special skills as determined by the chief of the clinic.

18 There should be good follow up on patients who had been in therapy but were temporarily terminated (to be on their own for a trial period).

19 Group therapy for patients should be conducted whenever feasible. It should be supplemented (when necessary) by individual treatment.

20 Scheduling should be done efficiently and economically to prevent unnecessary trips to the clinic especially during the diagnostic period (*For example* The history should be completed one week without the child being brought in, the parents and the child are then scheduled to come to the clinic during another week. The history and other data are made available to the examiners prior to their seeing the patients. If the psychologist is to examine the child he will be scheduled to do this while the parents are seen by the psychiatrist. The child may then be seen by the psychiatrist.)

21 In most instances of diagnostic study the clinical psychologist will examine the child the day that the psychiatrist interviews the parents. Thus at the staff conference there will be available medical history data and the current physical examination report plus reports by the social worker, psychiatrist and psychologist. Also the key family members will have been appraised by *at least two* staff members.

22 Expert consultants in child psychiatry and psychology should be available to the staff for teaching and consultation purposes (desirable but not mandatory).

## SUMMARY

The principles for child (and parent) guidance services in military medical installations include the establishment of (1) local need for such specialized services, (2) an awareness that the services do not duplicate those otherwise available, (3) organizational structure of this type of clinic, (4) basic staffing requirements and (5) essential liaison functions. There is need for long range record keeping, functionally effective interdisciplinary working relationships, and operating procedures that include attention to other members of a "patient's" family. Criteria for evaluation of a child guidance clinic are presented as guidelines both for establishing a clinic and for appraising one in operation.

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## OFFICIAL RECOGNITION OF MILITARY MEDICINE

I believe military medicine should be developed as a recognized specialty and given all the prestige and importance that can be given to it. At the same time the recognition of specialization as it is presently understood should be furthered. One of the fine things since the last war has been the program for the training of specialists within the services and the increased opportunity given to specialists to function in the framework of military medicine. I would advocate the organization of military medical men as a component part of the American Medical Association with status similar to a state medical society and with duly and democratically elected delegates to the house of delegates proportional to the number of doctors in the military services.

—RUSSEL V LEE M D  
in *Journal of the American Medical Association*  
p 807 Oct 19 1957



# SERVICE ARTICLE

## MARTIN ARMY HOSPITAL, FORT BENNING, GEORGIA

### Dedicatory Address

JAMES P. COONEY M, G I MC USA

SINCE the audience to which I am speaking today is chiefly composed of Fort Benning personnel and friends I shall spend little time on the history of what is often called and with good reason the Army's most complete post.

### THE PAST OF FORT BENNING

Fort Benning originated as Camp Benning on a few acres near Columbus, Georgia, in 1918. It became a permanent military establishment in 1922 and by 1939 when its real functional expansion began it had spread over almost 100,000 acres. During World War II it was the site of feverish military activity. Its expanded terrain of well over 200,000 acres made it as it still makes it admirably suited for all kinds of training. Infantry, airborne infantry, artillery, and armored units all trained here. Paratroopers learned both to jump and to fight. Young infantry officer candidates were graduated by the thousands. Army Specialized Training Program trainees were sent here. There was even a prison camp for Italian prisoners of war. The alumni of Fort Benning went to the far corners of the earth during World War II; they fought in the Korean Conflict and they are still serving their country in all parts of the world today.

In the early days of what was then Camp Benning, its personnel was served by a station hospital which was housed in one story temporary wooden structures. In 1924 a permanent hospital was completed. With two subsequent expansions, the original 10 beds were increased to 364. These hospital facilities were ample until 1939 when the prewar mobilization began. Then as the military population increased to 75,000 and then to 100,000 these facilities also were increased at first by improvisation then by new construction until the bed capacity was eventually more than 3,000.

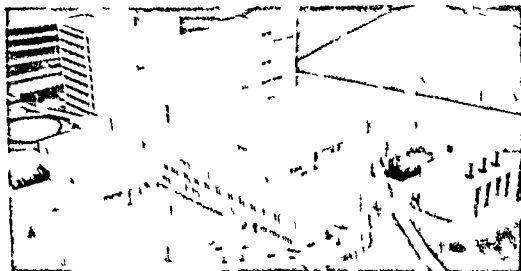
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Addressed 1 July 1958 to the ceremony of dedication of the new  
Deputy Surgeon General's Hospital to the Army

## THE NEW MARTIN ARMY HOSPITAL

The beautiful Martin Army Hospital which we are dedicating today is a far cry from the crowded hospital of 1914 and even from the new structures of World War II. In its fabric and equipment it represents all that is newest and most efficient in hospital construction including, as I am sure all of us gratefully acknowledge on this hot July day, its air conditioning system.

The 500 beds with which this hospital will begin to operate tomorrow can be expanded to 1,000 beds. This is a wise provision. Last year, the hospital facilities which are now being superseded cared for total admissions of 11,104 representing an average daily census of 478 and 170,115 stay days. There were 5,175 visits to the outpatient clinics, and the clinical laboratories performed the incredible total of 540,711 tests.



*Here is the new and better hospital.*

I mention these statistics deliberately. This hospital has been designated to train interns and postgraduate residents, and the clinical material, as you can see, is ample for this mission.

## MAJOR GENERAL JOSEPH I. MARTIN

For a great many years it has been the pleasant and well-deserved custom to name Army hospitals in the United States for great men in the Medical Corps and in other branches of the Army Medical Service. Major General Joseph I. Martin, in whose name it is my honor and privilege to participate in the dedication of this hospital today, was my friend, as I know he was the friend of many of you here. Let me recall to you some things about his long career in the Medical Corps and about the man himself.

I might begin with his remarkable ability to talk extemporaneously, yet so lucidly and so interestingly, that you realized that his remarks, which were sometimes quite extemporaneous, were actually

unprepared Since I do not possess his ability I will proceed with what a former Lord Chief Justice of England was in the habit of describing as his carefully prepared impromptus

General Martin never knew a medical life of which the Army was not a part He was commissioned as a first lieutenant in the Medical Corps of the Organized Reserve immediately after he was graduated from the Chicago Hospital College of Medicine in 1918 Two years later he was commissioned in the Regular Army Medical Corps



M J G I J phl Mart

His first assignments were those of any young medical officer after World War I not too many of them I imagine very exciting But they were well performed and significantly Captain Martin soon began to receive assignments for additional training In 1926 he was graduated from the basic course at the Army Medical School at Carlisle Barracks In 1928 he was graduated from the Advanced Course at the Infantry School here at Fort Benning In June 1934 as a major he was graduated from the two year course at the Command and General Staff School at Fort Leavenworth, Kansas and in June 1940 as a lieutenant colonel he was graduated from the Army War College in Washington

In the introduction to the story entitled "The Courageous Medics of Anzio,"\* published in *Military Medicine* this year, General Martin, in the foreword which he prepared shortly before his death, said that the medical officers who commanded there had developed their ability for their command as the result of long individual preparation and training. He might well have been writing of himself. All of his prewar assignments, a large number of which concerned medical education and training, prepared him for the responsible duties he was to assume during and after the war.

Those duties were impressive indeed. Surgeon, Fifth U S Army, in the North African (later Mediterranean) Theater of Operations, Chief Surgeon, Western Pacific, and, later, Surgeon, Army Forces in the Pacific Commandant Medical Field Service School, and Commanding General Brooke Army Medical Center, and Chief Surgeon, United States Army Forces Europe.

At Carlisle Barracks, when he attended the Army Medical School, General Martin was awarded the Skinner Gold Medal, which is presented annually to the student officer who is graduated with the highest scholastic average. It was the beginning of a long list of honors and decorations, including the Distinguished Service Medal, the Legion of Merit, the United States of America Typhus Commission Medal, and decorations from seven foreign countries among them the Most Excellent Order of the British Empire.

The citations are remarkably interesting. The Typhus Medal, for instance, was awarded to General Martin for his activities in the epidemic in Italy in 1943-1944 during which no American soldier contracted the disease, and the epidemic in Japan in 1946 in which he had much to do with preventing what could have been one of the world's greatest medical catastrophes. The citation for the Legion of Merit recalled his coordination of the services of the British and American components of the Fifth Army which also was recalled in the citation for the British order. The happy relations between the two medical forces wrote the Commander of the Fifteenth Army Group. General Sir Harold R. Alexander was due to General Martin's unfailing courtesy and consideration.

Similarly, I have found it extraordinarily interesting to follow General Martin's efficiency reports across the years. One of the earlier ones which concerned his proficiency in horsemanship carries the echoes of another day.

More seriously, he was described in the first report in 1920 as a young officer of great good sense. He was then at Camp Grant where, 20 years later, he was to do outstanding work in

the organization and functioning of the Medical Replacement Center. Always the emphasis is the same. This was an officer who put as much energy and interest into distasteful work as into work in which his particular interests lay. He had a marked aptitude for field work and training. He would be well fitted for the training and command of medical department units for field service. He was of very great present and potential value to the Army. He would be the right hand of any officer under whom he might serve.

Then came the war and the postwar years when in positions of high honor, trust, and enormous responsibility, General Martin's efficiency reports contain tribute after tribute, not only from the Medical Department officers who wrote them but from the line officers who countersigned them. Here are some of them:

He combined splendid soldierly qualities and qualities of leadership with excellent judgment. He was professionally competent and he was an outstanding authority on training and on the broad aspects of medical service in an overseas command. He was a superior administrator. He worked smoothly under adverse circumstances. *(The line officer who wrote that had seen him in action at Anzio.)* He was a creative thinker. He inspired respect, admiration, and loyalty. He was of immense value to the service and superbly qualified for any assignment.

I imagine that the efficiency rating General Martin probably cherished most of all was the one that described him as a blunt, sincere, direct, demanding officer who maintained a superior level of efficiency in his command. I think he must have cherished it because it was written by a line officer who had much of the same qualities himself. This officer was General Anthony C. McAuliffe, Commander in Chief, U. S. Army Forces Europe, the same General McAuliffe who some 10 years before had greeted the arrogant German demand for the surrender of the surrounded forces in Bastogne with the all-inclusive, absolutely final and typically American response, 'Nuts!' It is about the reply General Martin would have given had he been there.

Those of you who knew General Martin will remember him well. He was a big man physically, with a commanding presence and a booming voice. He took physical fitness and the techniques of accomplishing it as part of the day's work. He could take poor physical material and make something out of it. As another of his efficiency reports noted, he had done just that with basketball and football teams of enlisted men when he was a young instructor at Carlisle Barracks.

Because of his broad service and experience and his assignments as student instructor and later commanding general at the various service schools, General Martin had hundreds of friends in the line. They admired and respected him, and they

listened to what he had to say because they knew that his presentations were authoritative and were based on a complete knowledge of his field. He would have been a fine line officer himself. As it was, he added to the prestige of the Medical Department and increased its capabilities for service because of his relationship to officers of the line.

He was known to thousands of Medical Department officers, noncommissioned officers and enlisted men who regarded service under him as a privilege, though there was no more demanding officer in the Medical Corps. One reason was that this same demanding officer had another, gentler side. He was a man of deep religious convictions, who practiced his religion devoutly. He required the utmost of his men, but he had a deep understanding of human limitations and frailties and no man who was doing the best of which he was capable need fear General Martin's frown. Many one-time sergeants who had become commissioned officers during World War II furnished problems in assignment after the war, but not to General Martin. He accepted them in his command, and he utilized these fine old soldiers to the best of their abilities and to the good of the service.

#### THE IDEALS OF AN ARMY HOSPITAL

What would General Martin have wished of this hospital which bears his name and which serves among other establishments on the post the school in which he was once a student officer? He would demand professional competence of course. But I think he would also desire what a former President of the American College of Surgeons once well termed "the humanities of medicine."

As I have gone about from hospital to hospital in our world-wide Army Medical Service, I have been impressed again and again with the need for the practice of those humanities. We in the medical service must treat our patients as well as the diseases from which our patients suffer. We must approach their ills with kindly and sympathetic interest. We must remember, as Lord Moynihan once put it, that what to the physician is part of his daily life, to the patient and his loved ones may be the ordeal of a lifetime. If we bear these things always in mind, no detail of the care of a patient will be too small to be of concern to us.

This is the art of medicine. It should be practiced in all diseases, be they trivial or lethal. It holds for all who have any relationship at all with the patient and his family, be they medical officers, nurses, enlisted men, or civilian personnel. The art of medicine can be practiced, you know—and should be practiced—by the enlisted man with whom most patients in military hospitals have their first hospital contacts. It should be practiced by the dietitian, the physical therapist, the registrar, and the ambulance

driver to mention a few of our ancillary personnel. Some of the most gratifying comments we are receiving about medical care concern the kindness and thoughtfulness of these personnel and I hope that in this hospital they will always realize their responsibility for maintaining the honor of the Medical Corps. The art of medicine is made up as you see of little as well as big things.

Are the art and science of medicine incompatible? Not at all. Let me give you one or two illustrations.

Take William Beaumont whose faithful performance of what he called the common avocations of life and professional duties prepared him so admirably to make the observations on gastric physiology which are the basis of all modern concepts in that field and which were possible when opportunity came his way in the person of "old fistulous Alex."

Take Sir James Mackenzie. His title came late. He was for most of his life a country doctor with little medical education and with no laboratory personnel or equipment to help him but no man has ever contributed more to the science of cardiology. He accomplished it simply by observation of his own patients over years and years and years and by the careful recording and correlation of these observations. To the end of his days his biographer recalled he wore the title of family doctor as if it were a plume.

Take Harvey Cushing the pioneer and founder of modern neurosurgery. His biographer the distinguished physiologist John F. Fulton wrote of him

By valor and discipline and he had more than fulfilled the promise and ambition of his youth: scientist, pathfinder, artist, writer and bibliophile—ye but above all a good doctor.

A recent President of the American College of Surgeons wrote his Presidential Address around that theme. But above all a good doctor.

Finally take Sir William Osler. His academic education and medical training were of course superior. Before his life ended there was scarcely a disease to which he had not added some illuminating observation. Yet one thing that he always told his students and residents was that they must have regard for the rights of patients by which of course he meant far more than the legalistic implications of the term. To him the rights of patients included the human kindness, the sympathy and the compassion which I plead with you to make the hallmarks of this new hospital. In this scientific age they are sometimes forgotten. Osler never forgot. It was said of him that he never left a sickroom without leaving renewed hope behind him. He was the living embodiment of something Stephen Paget once said that to

be wanted by men and women, to come natural to them in time of trouble, might fairly be called a career

Among Osler's letters is one written early in his practice to the father of a young man who had died of smallpox in Montreal. He told all the particulars of the son's illness, and we may be certain that the patient had from the young physician the best care that medical science could then provide. But Osler also told the bereft father how he had read to him from the Bible the young man's mother had marked for him and, he concluded "I performed the last office of Christian friendliness I could and read the commendatory prayers at his departure." How it must have comforted those stricken parents to know that their dying son, a stranger in a far land, had gone into the farther country with his hand in the hand of this gentle and kindly physician.

Osler never lost that kindness. Many years later, when he was Sir William Osler and Regius Professor of Medicine at Oxford, shortly before his own beloved and only son fell in battle, he wrote another grieving mother of how the night before he died, her young soldier son had asked to be alone with him, and, he said, "I did what I could to comfort him." No physician ever lived in whom the science and the art of medicine were more happily combined.

It was in 1899 that Letterman General Hospital in San Francisco became the first Army hospital to bear the name of a former medical officer. The hospital which we are dedicating today becomes the sixty fifth to bear the name of some officer in the Regular or Reserve Army Medical Service or some related arm who, as the memorialization criteria express it, "has distinguished himself by serving in or with" the branch in which the installation has been set up.

I knew General Martin personally. I have also known some of these other officers during my service in the Medical Corps. Some of them I know only from their records. But one thing I know about them all. They have all of them done well by their country. And as I recollect the hospitals which bear their names—I have had some personal contact with almost all of them—I realize that these hospitals and their personnel also have done well by the country.

This hospital beautiful, new and modern in every respect, will I know, continue to build upon the honorable traditions of the medical service that has been provided here since Fort Benning was first established 40 years ago. I can wish for this new hospital nothing better than that it should carry on in its own tradition and in the tradition of the other hospitals which, like it, bear the honored names of former medical officers. I know that the gallant and distinguished officer whose name it will bear could wish nothing better for it. And I know that he would wish for it as I do, that its record of human kindness should be as great as I am sure its record of scientific achievement will be.





## Clinicopathologic Conference

U S Naval Hospital St Alban N Y

### FEVER AND HEPATOMEGALY

**Summary of Clinic History** A 55 year old retired Army officer noticed two abdominal masses two years prior to his first hospital admission. One mass was on the left side of the abdomen the other in the epigastrium both had gradually increased in size and were occasionally tender. The patient was known to have had (1) pleurisy on the right side in childhood (2) an appendectomy in 1925 (3) a tonsillectomy in 1940 (4) malaria in 1944 and 1946 treated with Atabrine (brand of quinacrine hydrochloride) (5) fracture of the lumbosacral spine with disk herniation in World War II (6) rectal polyps removed by sigmoidoscopy in 1946 and (7) a fibroid tumor removed from the right forearm a few weeks prior to admission. He was a lawyer and had served in Africa and Korea.

### FIRST ADMISSION

On 11 August 1955 the patient was admitted to this hospital with chief complaints of abdominal pain weakness and melena of one week duration plus the known abdominal masses. His pain was aching most marked in the right upper quadrant and epigastrium not related to food ingestion (except for relief following milk) and accompanied by anorexia. Although the patient denied alcoholism his family told of frequent ingestion of alcohol.

**Physical Examination** The patient was a well developed well nourished man who appeared chronically ill and anemic but in no acute distress. His temperature was 99.4 F pulse 108 blood pressure 160/104 mm Hg and respirations 20 per minute.

C pt. H ma A G MC USN Command g Off F m h Laboratory  
 Serv C pt. Sark S Sak MC USN Ch f

The abdomen was flat and soft, with a mass thought to be spleen in the left upper quadrant, and an epigastric mass thought to be liver. Both masses were tender. The prostate was minimally enlarged. There was tenderness over the lumbosacral spine with straightening, and rigidity of the lumbar curve. The remainder of the physical examination was negative.

**Laboratory Studies.** Examination of the blood revealed a red blood cell count of 2,330,000 per  $\mu$ l, a hemoglobin of 6 grams per 100 ml, and a hematocrit of 22 ml per 100 ml. Sedimentation rate was 30 mm per hour (corrected). The white blood cell count was 6,050 per  $\mu$ l with 80 per cent neutrophils, 1 per cent band forms, 17 per cent lymphocytes, 1 per cent monocytes, and 1 per cent eosinophils. The platelet count was 123,490 per  $\mu$ l. Bilirubin was 0.5 mg per 100 ml, total proteins, 6.0 grams (3.0 grams albumin, and 3.0 grams globulin) per 100 ml. Sulfobromophthalein sodium retention was 15 per cent in one hour. Serum amylase was 416 units, thymol turbidity, 5.9 units, alkaline phosphatase 12.1 King Armstrong units, and the cephalin cholesterol flocculation test was negative. A Coombs test was negative.

A roentgenogram of the chest disclosed no abnormalities. A gastrointestinal series revealed an enlarged spleen which displaced the stomach to the right and the right kidney medially and downward. An extrinsic pressure defect was demonstrated on both the greater curvature of the stomach and the duodenal cap. A cobblestone appearance of the cardia suggested varicosities. An esophogram showed large varicosities extending from the lower half of the esophagus to the level of the tracheal bifurcation. An intravenous pyelogram was normal. Films of the lumbosacral spine were consistent with hypertrophic arthritis.

**Course in Hospital.** Repeated blood transfusions raised the red blood cell indexes to normal. Liver biopsy showed portal cirrhosis. Bone marrow examination was normal. Rectum to arm circulation time using sodium<sup>24</sup>, was 90 seconds (consistent with increased portal vein pressure). Two months after admission a splenorenal shunt was performed, with concomitant splenectomy. At operation the liver was described as small and nodular. Initial omental venous pressure was 360 mm of water, and after completion of the shunt the pressure fell to 300 mm of water. The patient tolerated the procedure well and post-operatively his anemia did not return. However, he developed a low grade fever, which was present on discharge. Two months later, on return outpatient visit his rectum to arm circulation time was 33 seconds (consistent with a patent shunt).

#### SECOND ADMISSION

The patient was readmitted on 10 June 1956, complaining of fever and left upper quadrant pain. Since discharge he had experienced continuous fever with spikes up to 104°F.

**Physical Examination** The patient was alert co-operative and did not appear to be in acute distress His temperature was 100.2 F pulse 88 blood pressure 148/56 mm Hg and respirations were 16 per minute Large soft submandibular lymph nodes were noted bilaterally The abdomen was soft There was a curved linear scar on the right flank and a hockey stick scar on the left flank and back There was mild tenderness in the left upper quadrant The liver was firm and was palpable four fingersbreadth below the right costal margin The flanks appeared full but without ascites The lumbosacral spine was tender Physical examination was otherwise negative

**Laboratory Studies** Complete blood cell counts were within normal limits Urine sediment contained from 2 to 4 white and 2 to 4 red blood cells per high power field Serum albumin was 3.6 and serum globulin was 4.6 grams per 100 ml Alkaline phosphatase was 10 and acid phosphatase was 2.5 king Armstrong units Thymol turbidity was 10.2 units Cephalin cholesterol flocculation febrile agglutinins and repeated blood cultures were negative Neither ova nor parasites were found in many stool specimens Malaria parasites were absent from smears Bone marrow examination was normal

Roentgenograms of the chest and abdomen revealed no abnormalities those of the gastrointestinal tract showed progressively enlarging varices of the esophagus An intravenous pyelogram disclosed no abnormalities

**Course in Hospital** The patient gradually developed ascites and anemia He was given a course of emetine hydrochloride and chloroquine phosphate in spite of the absence of demonstrable parasitic infestation but his febrile course was unaltered On 15 August two months after his second admission exploratory laparotomy was performed At exploration the shunt was believed to be patent Pressure in the omental vein was 300 mm of water The patient tolerated exploration well but continued febrile with occasional spikes to 104 F On 25 September he had massive hematemesis controlled by passage of a Blakemore tube and blood replacement Nine days later he died following another massive hematemesis

## DISCUSSION

**Diagnosis** The problem presented by this patient is the explanation for the continuous fever that was present since the patient had an operation for portal hypertension Two very enticing possibilities immediately arise one from the present and the other from the present history The patient had malaria on two occasions could this present pyrexia be due to a recurrence of malaria? Not very likely for we are told that repeated examinations for malarial parasites were all negative The course of the fever is not typical for this was a prolonged continuous fever over a 10-month period

Thrombo-lysis or fibrinolysis is a process by which the blood clots are broken down. It is a natural process that occurs in the body. The process involves the release of plasminogen activators (tissue plasminogen activator and urokinase) from the endothelial cells of the blood vessels. These activators convert plasminogen to plasmin, which then breaks down the fibrin meshwork of the blood clot. The process is regulated by various factors, including the presence of fibrin, the concentration of plasminogen, and the activity of the plasminogen activators. Thrombo-lysis is a critical process for maintaining blood flow and preventing thrombotic events. It is also the basis for many thrombolytic therapies used to treat acute myocardial infarction, stroke, and other thrombotic conditions.

From the report of the patient it was concluded that the  
 evidence by the patient of the presence of a tumor in the  
 should be sufficient to warrant a biopsy of the tumor in the  
 noma of the tumor. The patient should be ruled out as a  
 lesion. The patient should be ruled out as a lesion, consti-  
 tuting a tumor of the tumor. The patient should be ruled out  
 and the patient should be ruled out. Finally, a therapeutic  
 was done by the patient.

The present picture can be due to him to Africa and the disease must be considered. Schistosomiasis must be ruled out here from stools with reason to find ova and parasites. Schistosomiasis and Schistosomiasis japonicum can both cause such a clinical picture with the former more likely, because *S. japonicum* usually produces a more severe acute disease but may carry on to the stage of hepatic cirrhosis. *S. mansoni* commonly produces a clinical picture with hematemesis from esophageal varices as the terminal event. The initial infection may be overlooked.

Infections such as tuberculosis typhoid fever and brucella must be considered in all unexplained fevers. We are told that washings and agglutination tests were negative.

Lymphoma is another possibility in unexplained fevers. But this examination did not reveal any significant adenopathy. Blood counts and bone marrow examinations likewise were not suggestive. The fever was not of a Pel-Ebstein type which incidentally is commonly found in proven cases of Hodgkin's disease. Percussionograms of the chest did not reveal any mediastinal widening and may be the first sign of lymphoma. No intra-abdominal masses apart from the enlarged liver were palpated. Uric acid and serum calcium determinations would have been helpful for hyperuricemia may result from increased catabolism while hypercalcemia may reflect tumor involvement with tumor. Lacking substantiating evidence however, lymphoma may be dismissed.

Other malignant processes might be considered. In this case the possibility of hepatoma is interesting. Primary carcinoma of the liver occurs in about 8 per cent of all cases of cirrhosis. It commonly produces a persistent irregular fever which may be caused by necrosis of the tumor nodule. If in a patient with cirrhosis a careful search for other causes of fever is unproductive then hepatoma must be near the top of the list of causes. Liver biopsy may be helpful.

the operator is so fortunate as to biopsy a malignant focus. Ascites in a patient with cirrhosis and with ut hypoalbuminemia is suggestive of hepatoma. A marked elevation of the alkaline phosphatase without accompanying jaundice is also suggestive of hepatoma. Ascitic fluid should be examined for malignant cells.

The cause of death in this patient was probably a result of the hematemesis. As for the continuous fever I shall put hepatoma first and chronic chistosomiasis as the next best cause.

**Discussion.** When this patient was first seen by physicians from the surgical service he fulfilled the criteria of what would be considered a good candidate for a shunting procedure. The history of a heavy alcoholic intake together with the physical and laboratory findings including a liver biopsy consistent with Laennec's cirrhosis left little doubt as to the cause of his portal obstruction. The roentgenographic evidence of large varices of the lower esophagus and cardia of the stomach together with the elevated rectum-to-arm circulation time, splenomegaly and hyperplenism reflected an elevated portal pressure. The cause of the obstruction, the resultant portal hypertension and the evidence of bleeding from the varices were then manifest. With no ascites, a negative cephalin flocculation, a serum albumin of 3 grams and only moderately elevated sulfobromophthalcin retent on the patient was considered a good operative risk for a shunting procedure. The decision remained then only as to choice of shunt. A markedly enlarged spleen and evidence of hypersplenism were the deciding factors in performing a splenorenal anastomosis. The removal of the spleen would relieve the symptoms of hypersplenism as well as decrease the portal blood volume by an estimated 40 per cent.

The fact that the omental venous pressure dropped only from 360 mm to 300 mm of water after the shunting was completed is not an unusual finding. The decrease in the size of the varices and the drop in portal venous pressure are gradual processes and it takes an estimated several hours before the body accommodates to this shunting procedure. The normal rectum to arm circulation time two months postoperatively indicated to us that the shunt was patent at that time. The possibility of a hepatoma was considered by members of the surgical service but this was never confirmed by several deep-needle biopsies in various quadrants of the liver. This however did not negate our suspicions. The increased incidence of a hepatoma in a cirrhotic liver is well known.

In view of the patient's symptoms of left upper quadrant tenderness and febrile course a limited abdominal exploration was performed to determine if an abscess was present. No infection was found at time of operation and the liver was not palpated.

This case illustrates one of the major disadvantages of a splenorenal anastomosis. For reasons not well known possibly due to the age

of the anastomosis of superior vena cava to inferior vena cava  
the anastomosis was not found.

### Clinical diagnosis:

- 1 Portal cirrhosis
- 2 Hematuria
- 3 Esophageal varices
- 4 Schistosomiasis

### POST-MORTEM FINDINGS

Dr. Hyams: The patient was a well-nourished man of moderate build. The sclerae were icteric. The abdomen was protuberant. The legs revealed a 1-plus pitting edema of the feet. The thoracic cage contained approximately 100 ml of blood-tinged fluid in both pleural cavities. The heart was normal on gross examination. The lungs contained a small amount of red fluid in the dependent portions. The peritoneal cavity contained approximately 1000 ml of clear, straw-colored fluid. The spleen was absent. There was only a small, healed linear scar with remnants of black ink suture in the left renal vein. The spleen was not identified. The liver weighed 2300 grams and was of normal shape. The external surface had a tan, markedly nodular appearance (fig 1) with the exception of the inferior surface of the right lobe where there was a large, rounded, tan-colored protruding mass that was 12 cm in diameter. The cut surface of the liver revealed the typical Laennec's appearance except in the right lobe (fig 2). The center of this lobe was replaced by a pinkish white caseous mass which appeared to be circumscribed by a thin band that resembled fibrous tissue. The stomach contained 1500 ml of dark red blood, and the intestine was filled with old blood. A ruptured varix was identified in the lower part of the esophagus. The remaining findings were normal. Microscopically, except in the area of the right lobe where there was mainly caseous necrotic material, the liver showed a picture of portal (Laennec's) cirrhosis. However, there were occasional small islands (fig 3) composed of cords of normal hepatic cells but showing marked pleomorphism, hyperchromatism of the nuclei, as well as an increased number of cytoplasmic borders and numerous mitotic figures. These findings were characteristic of a hepatocarcinoma. The remaining microscopic findings were pulmonary congestion, atrophy of testes, and chronic cystitis.

In recapitulating the case, the diagnosis of massive gastrointestinal hemorrhage for a ruptured varix as a consequence of long-standing portal hypertension.

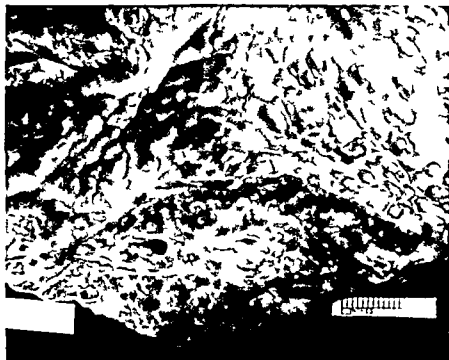


Figure 1. External surface of the right lobe of the placenta.



Figure 2. Cut surface of the right lobe of the placenta.



Figure 3 Photomicrograph of hepatoma. ( $\times 200$ )

above course and termination is the usual picture in portal cirrhosis. The finding of hepatocarcinoma in cirrhosis of the liver is not unusual, and in the clinical picture of this patient with an unexplained fever hepatocarcinoma should be considered.

**Pathologic diagnoses**

- 1 Hepatocarcinoma
- 2 Cirrhosis portal
- 3 Pulmonary edema bilateral with aspiration of recent hemorrhage
- 4 Bleeding esophageal varices with massive gastrointestinal hemorrhage



pathologic lesion vision visual fields and fundi were normal and it was thought that his symptoms might have been due to arteriospasm of the retinal vessels. As on previous occasions all his symptoms subsided after a few days and a week later he was reassured and discharged.

For over three months the patient felt well and did not call at the hospital. When his symptoms recurred he was advised to see either a psychiatrist or a cardiologist for a second opinion. He decided in favor of the cardiologist but expressed a willingness to see a psychiatrist later if thought necessary. The consulting cardiologist reassured the patient that no organic cardiac disease was present and in his medical report stated that he believed that the patient's complaints were due to a vasovagal syndrome though at the beginning of his illness he might have experienced attacks of paroxysmal tachycardia. For the next two weeks the patient was well and felt on top of the world. It had all been in my mind and maybe I read too much about heart diseases. were now his frequent remarks. He disclosed that when a friend of his had died suddenly of a heart attack he began to read about heart diseases. After this short asymptomatic period he suddenly started to complain of frequent attacks of sharp precordial pain which came on whilst walking only a short distance as well as at rest at home. It was the first time that he had described a definite pain and not only a discomfort. The pain started in the epigastrium radiated upward to both sides of his chest and responded to glyceryl trinitrate.

Ten days later in March 1956 the patient had to be readmitted for the fourth time by ambulance after his office telephoned that he was in severe pain and unable to walk to the hospital a distance of 200 yards. He looked pale with a slight malar flush and was apparently in great pain. He clutched his chest with cold clammy cyanotic hands and there was perspiration on his forehead. The pupils were widely dilated. His pulse rate fluctuated between 84 and 120 its rhythm was regular heart sounds were normal and there were no murmurs pericardial rub or abnormal accentuation. Respiration was normal and there was no evidence of pulmonary congestion. Blood pressure was 135/85 mm Hg. The attack had started half an hour previously and had not responded to glyceryl trinitrate. The patient had at first thought that he had an attack of indigestion but later the pain extended toward the lower end of the sternum radiating toward his left shoulder and down his left arm. Morphine 0.016 grms was given intramuscularly after which the patient fell asleep. Next morning apart from a slight feeling of general weakness the patient felt and looked perfectly well and did not complain of any pain. An electrocardiogram however revealed for the first time deep depresseion of the RST segments in limb and precordial leads most marked in I, II, V<sub>1</sub>, V<sub>4</sub>, and V<sub>6</sub> and elevation of RST in aVR and V<sub>1</sub> suggesting diffuse myocardial ischemia. No Q waves were seen and T waves were upright except in aVR (fig 1 B and D). Twenty four hours later a perfectly normal tracing was recorded and all RST deviations had subsided.

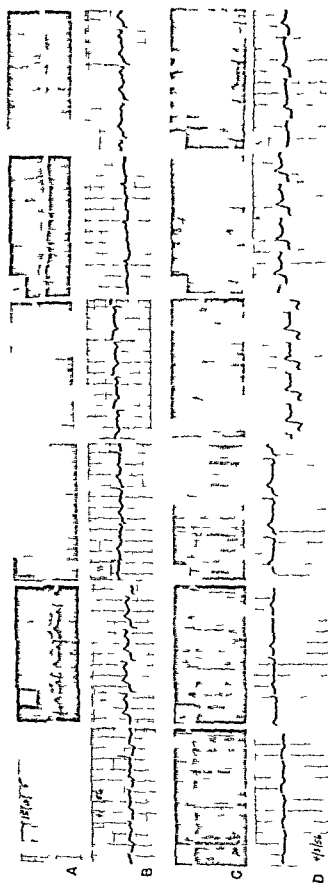


Figure 1 A and C show normal electrocardiogram taken on 15 October 1955. B and D show ST depression present on 14 May 1956 the day following a severe episode of precordial pain.

The patient was kept in bed and was given sedatives and glyceryl trinitrate with instructions to suck one tablet in case of recurrence of the pain. An oxygen cylinder and cardiograph were placed near his bedside. He admitted now that he had been living under considerable mental and physical strain for several years. He disclosed serious domestic and financial difficulties as well as friction at his work. The latter had even led to a court martial proceeding. He thought he had noticed that his superiors had become dissatisfied with his work and from his story a good deal of repressed hostility, fear, and severe anxiety with even some psychotic-paranoid features appeared to emerge. It was now thought that his anxiety state had reached such a degree that it had become responsible for attacks of coronary spasm and transient myocardial ischemia. The normal tracing 24 hours after the precordial pain had subsided seemed to confirm such a view. The patient, however, experienced more frequent attacks of precordial pain at rest in bed which came on during the day and night. The pain lasted only a few minutes and responded to glyceryl trinitrate. The patient had now become so frightened of these attacks that he took glyceryl trinitrate whenever he felt that a pain was imminent and it therefore became impossible to take an electrocardiogram actually during an attack. Those tracings that were taken after one showed a degree of myocardial ischemia though in none of them were the changes found to be as marked as in the first one after admission. The mere recording of his blood pressure or the auscultation of his heart seemed to bring on an attack and this was usually associated with flushing of his face, frequent blinking of his closed eyelids, and a nervous finger-nag of the sternal area. One day when he had felt comparatively well he suggested bringing on an attack at will so that a tracing could be taken during the pain. He added that he had only to think of some of his worries in order to provoke precordial pain. Throughout this stay in the hospital his temperature, white blood cell count, and sedimentation rate had remained normal.

On the seventh day of this last admission he woke up at 0300 hours, asked for the oxygen mask, and died within 3 minutes.

#### POSTMORTEM EXAMINATION

**Gross findings.** The heart weighed 360 grams. The myocardium was dull red and moderately flabby. The epicardium was smooth and glistening. The myocardium of the left ventricle measured 14 mm in thickness and that of the right ventricle 5 mm. The cavities of the heart were slightly dilated and contained clotted blood. There were no palpable areas of myocardial softening. The endocardium was smooth and glistening throughout. The intima of the coronary arteries showed a few yellow nonobstructive plaques with the exception of a single plaque near the beginning of the descending branch of the left coronary artery. This plaque bulged into the lumen of the coronary vessel to reduce its internal diameter one third to one half of normal. The aorta showed good elasticity without intimal plaques without calcification.

fication or ulceration. A detailed examination of all organs in the thoracic and abdominal cavities including the adrenal glands failed to show any abnormality.

**Anatomic diagnosis** Localized obstruction of a coronary artery

**Histologic findings** Sections taken through a segment of coronary artery revealed thickening of the subintimal layers of the vessel by a pale basophilic type of connective tissue (fig. 2). In some areas the matrix of the connective tissue showed a fibrillar or mucoid type of degeneration and in these areas nuclei were largely absent or pyknotic. There was no evidence of ulceration of the intima, thrombosis, inflammatory cell exudate or hemorrhage within the wall of the vessel.

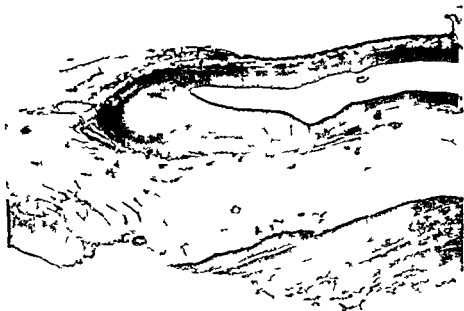


Fig. 2. Intimal thickening of descending branch of left coronary artery (hematoxylin and eosin stain  $\times 55$ ).

Sections of heart muscle and sections through the atrium and ventricle including a portion of one of the heart valves revealed normal endocardium, muscle fibers, and nuclei. Striations were evident on many of the muscle fibers. There was no apparent increase in fibrous tissue between muscle fibers in this section. The heart muscle showed fat cells within the pericardium extending somewhat into the myocardium between muscle fibers. This represented a mild degree of lipomatosis. There was no evidence of fatty degeneration of muscle fibers.

Further sections revealed a vessel within the pericardium showing increase in fibrous like tissue of the subintimal layers. Much of the media of the vessel showed a degenerative type of intercellular material rather than muscle fibers. There was no evidence of thrombosis, ulceration of the intima or hemorrhage within the wall of the vessel.

Within the myocardium beneath this vessel there was some increase in fibrous tissue between muscle fibers. There was no inflammatory cell exudate in this section (fig 3). Sections of the aorta revealed normal intima. The media of the vessel was formed of elastic fibers in the usual amount and distribution.

**Microscopic diagnosis:** Mild unobstructive coronary atherosclerosis with a single plaque in descending branch of anterior coronary artery reducing its bore by one half.



Figure 3. A section of the anterior descending coronary artery showing atherosclerosis. (X 90)

### DISCUSSION

The intimate relationship between the feeling of anxiety and sensations arising from the heart has long been emphasized by psychiatrists. These sensations may vary in intensity from slight precordial uneasiness accompanying mild anxiety states, such as that experienced by a motorist when he is halted by a traffic policeman to the intense "angor animi" that characterizes a severe attack of coronary thrombosis. It is said that John Hunter's terminal attack was due to anger for he took exception to the fact that the appointments committee at one of the London teaching hospitals would not give a vacant position to a Scottish protégé of his. The fact that fear and/or anxiety frequently aggravates an already impaired coronary circulation is well known and universally accepted. Here concentration on the heart may suffice to provoke a feeling of anxiety in predisposed individuals and is usually associated with an uneasiness under the sternum or left inframammary region. Whether intense and prolonged fear

can, in fact, lead to attacks of coronary insufficiency manifested by cardiac pain and demonstrated by RST segment changes in patients who were believed not to suffer from heart disease is still unproven, and indeed is unlikely.

It has become clear, however, that whatever the condition of the heart may be, the effect most closely associated with the heart is anxiety. A diseased cardiovascular system can produce anxiety just as anxiety is frequently a precipitating factor in cardiac symptoms. In other words, we are dealing with a typical vicious circle.

Klemperer<sup>1</sup> described emotion as an etiologic factor in organic heart disease and stated: "Modern medicine does not doubt that emotion can lead to cardiac death, but it has doubted whether joy and pain can paralyze a normal heart or whether a serious heart disease must not have been present before a strong effect can lead to sudden death. He asked whether a lasting emotion can so disturb a previously healthy heart as ultimately to threaten death, and after he cited a series of cases he answered this question in the affirmative. It was his opinion the finding of myocardial lesions in these cases is not against a psychogenic etiology and he explained them as the result of coronary spasm and resulting myocardial ischemia."

Friedberg<sup>2</sup> termed the wide range which exists between the coronary flow under basal conditions and the augmented flow, when requirements of the myocardium are maximal, "the coronary reserve." This reserve may diminish or even become exhausted, not only by physiopathologic processes but also through psychogenic causes. In fear and excitement the physiologic power to augment the coronary flow by reducing the resistance or by dilating the coronary vessels whenever there is need for such compensatory adjustments may be impaired or totally lost.

Fahrenkamp like so many other observers rejected the old term of "pseudo angina" or "angina pectoris vera and falsa" and wrote:

There are intra vitam all possible transitional stages from the slightest disturbance of function in coronary circulation to the gravest pathological anatomical changes of the coronary vessels. Next to physical exertion psychic excitement is most likely to precipitate an attack. The greatest sense of annihilation with fear of death occurs chiefly in the second group because psychic excitement so often produces the first attack. Patient and physician may be inclined to consider the condition as nervous if the organic findings are slight but even the non neurotic patient may retain such a degree of fear of death from his first attack that he is unable to free himself from a secret anxiety.<sup>3</sup>

Master Jaffe and Field stated that hearing of a death, heated argument, shock, hemorrhage, vasovagal syncope, et cetera, may be responsible for an acute attack of coronary insufficiency caused by spasm or inadequate dilatation of the coronary vessels though some degree of coronary sclerosis and/or narrowing of these vessels may be found. Recovery in these cases is usually complete but it depends to a great extent on the inducing factor and on the degree of any underlying coronary pathology. The condition may be acute and very transient or it may last for many days or weeks in more severe cases. Electrocardiograms in mild cases may show no changes at all and no systemic signs such as fever, leukocytosis, or acceleration of the sedimentation rate will occur. Usually however, transitory RS T depressions and/or T wave inversion appear and may persist for days and weeks. Fatalities have been reported in less than 5 per cent of cases of coronary insufficiency and death is probably caused by an abrupt onset of ventricular fibrillation. Post-mortem examination usually reveals subendocardial necrosis or multiple small areas of fibrosis with or without some degree of coronary sclerosis.

Fast and Oram observed a large number of patients who experienced cardiac pain at rest lasting for more than half an hour but this was at first and on more than one occasion accompanied by perfectly normal electrocardiograms. Later transient T wave changes usually developed but without RS T segment displacements and of course without Q waves. They believed that the cardiac pain and transient T wave changes were due to prolonged coronary spasm affecting the left coronary artery much more frequently than the right. They further assumed that the reduction in the caliber of the vessel is not sufficient in degree or duration to give rise to significant myocardial changes. Prompted by these findings the same authors also drew attention to the error of assuming that a patient with precordial pain accompanied by a normal electrocardiogram cannot be suffering from true cardiac pain.

In his discussion of angina Houston<sup>6</sup> also mentioned the importance of neurogenic stimuli and he believed that if the pasmogenic aptitude is great even a slight stimulus will suffice to evoke the spasm with its characteristic pain.

More recently Evans<sup>7</sup> discussed 10 distinctive tracings which he found among 1,340 patients whose symptoms suggested cardiac pain. These recordings revealed T wave inversion in leads CR to CP and often also as far as CR and in L. In eight of these 10 cases the tracings reverted to normal while in the remaining two only slight abnormalities persisted. Evans too mentioned the absence of significant Q waves and of RS T segment deviations and pointed out that when the tracing had recovered, strenuous physical exercise will reintroduce the deformity un-

less a long pain free interval existed he suggested that such distinctive tracings of patients subject to cardiac pain should be named "mutable electrocardiograms" and he believed that they indicate coronary arteriospasm with temporary cardiac ischemia rather than lasting coronary occlusion with cardiac infarction. While Fast and Oram observed that the cardiographic changes always indicated a spasm of the left coronary artery, Evans went a step further and even localized the actual site of the spasm in the left coronary artery, distal to its circumflex branch and proximal to the left marginal branch unless it originates from the left circumflex artery. He suggested naming this segment of the coronary circulation "which possesses such a special aptitude to spasm 'the coronary floodgate,' for it can suddenly close and interrupt the blood supply to a large area of the heart and as readily it can open and re-establish the circulation." No mention was made of the emotional state of patients who exhibited these "mutable cardiograms."

An interesting observation was made by Berman, Simonson, and Heron<sup>8</sup> who studied the electrocardiographic effects associated with hypnotic suggestions in normal and coronary sclerotic individuals. Hypnotically induced states of anxiety, fear and work pain were studied on 14 normal young people and 11 patients with varying degrees of coronary artery disease. Electrocardiograms were recorded before and during the hypnotic states. In the normal group either type of suggestion produced T wave changes in 7 cases (50 per cent), elevation in 2 and depression in 5. In the group with coronary artery disease, 4 cases (36 per cent) showed T wave changes, elevation in 1 and inversion in 3. These results indicate that nervous factors may aggravate an already existing predisposition to ischemic cardiac disease. Observers point out that the emotional state should be considered in interpreting cardiograms in clinically healthy individuals.

Mainzer and Krause<sup>9</sup> reported abnormal electrocardiograms which were taken on people on the operating table immediately before induction of general anesthesia. These "fear recordings" revealed accentuation of already existing changes in patients with cardiac disorders but they also occurred frequently in persons who had had a normal tracing the previous day. The alterations were transient but sometimes they could still be observed 24 hours after operation. The authors classified them in three groups: (1) S T depression with low inverted or absent T waves; (2) P and T waves high and sharply pointed; and (3) a combination of (1) and (2). These observers believed that the tracings of group 1 indicated a reduced coronary flow due to vagal stimulation, that those of group 2 were due to a sympathetic over activity while the appearances of group 3 were thought to be



the result of the interaction of both factors. They suggested that cardiac death on the operating table immediately before the induction of general anesthesia as well as during anesthesia should at least in some cases be considered as the extreme outcome of an otherwise normal fear reaction.

Werley examined a series of case histories in which the picture presented was that of organic heart disease and where he believed that heart disease was in fact not present. In his opinion it makes no difference if a highly sensitive coronary artery gets into spasm because of emotion or because of an overloaded stomach or physical exertion. The symptoms will always be the same except for the emotional element or its absence. He further believed that even in true angina due to coronary sclerosis the attack may be precipitated by emotional excitement and he found that the result is very similar whether coronary arteriospasm is brought about by local organic disease or by overaction of the sympathetic system under the drive of emotion.

Once a person whose emotional reactions are disturbed and who is suffering from precordial pain has convinced himself that his pain is due to serious heart disease then a new and much more damaging fear is added, namely the fear of imminent sudden death. Various complicated conditioned reflexes, superimposed on this fear and anxiety state may not develop and finally it may become extremely difficult to distinguish between these distressing autonomic reactions and underlying heart disease. Tachycardia, transient elevation of blood pressure, dyspnea, perspiration, dilatation of pupils, transient visual disturbances (such as amaurosis fugax), Reynaud's syndrome, et cetera may all accompany precordial pain and represent vasomotor disturbances associated with an anxiety state.

Scherf and Boyd observed a patient in whom marked pallor of the entire left arm appeared simultaneously with an increase of blood pressure (blood pressure crisis) and angina pectoris. Stimulation of the cervical sympathetic during an attack of precordial pain was observed by Miller and Daley<sup>1</sup> who reported a case which exhibited lacrimation, sweating and vasodilatation of the left side of the face with dilatation of the left pupil and transient ptosis. A voluntary change in the heart rate, particularly acceleration, is still a controversial point. It may develop purely voluntarily or be indirectly produced by an emotional state. Voluntary slowing of the heart rate also has been observed in one by merely concentrating on a sad situation.

Stevenson and Duncan<sup>2</sup> described two major patterns of cardiovascular response to stress in individuals with cardiovascular disease. They associated one with mobilization for action characterized by increased cardiac output as a result of increase in rate and stroke volume combined with lowering of the pe-

peripheral resistance and slight raising of blood pressure. The second is cardiovascular hypoactivity: diminution in heart rate, stroke volume, and fall of blood pressure. They also observed rapid changes in the electrocardiogram including changes in the amplitude and direction of the T wave occurring in association with changes in the feeling state. Wolf and Wolff<sup>1</sup> were of the opinion that "heart pain in the presence of anatomic narrowing of the coronary arteries may result from increased work of the heart attendant upon prolonged elevation of the blood pressure and cardiac output in association with rage, resentment, anxiety, fear and tension, but they also believed that "heart pain may result from a fall in the cardiac output and coronary blood flow in association with desperation and defeat." They refer to the latter as the "hypodynamic response."

### SUMMARY AND CONCLUSIONS

The case of a 41 year-old man, who for almost five years was followed at this hospital for symptoms of progressive psychoneurosis, is reported. Cardiac investigations were persistently negative. The sudden cardiac death of a friend and his subsequent "interest" in heart diseases aggravated his mental condition and unleashed a number of vasomotor symptoms which convinced the patient that death was imminent. He eventually developed true cardiac pain and his electrocardiograms for the first time confirmed myocardial ischemia. The patient died in one of these attacks in bed, but a post mortem examination failed to reveal coronary occlusion, thrombosis or myocardial infarction. There was, however, some narrowing at one localized area of the descending branch of the left coronary artery by a single atheromatous plaque. Histologic slides revealed minimal, probably incidental myocardial fibrosis in the left ventricle.

Some of the literature dealing with the psychosomatic relationship in precordial pain and the changes in the electrocardiograms of emotionally disturbed people, as well as the electrocardiographic findings in coronary spasm and coronary insufficiency, is discussed. If one considers the history of this case and its unusual and bizarre symptoms, there can be little doubt that a severe progressive psychoneurosis existed. For almost five years his mental disturbance was manifested at first by hypochondriacal complaints, but later, after he had heard of the sudden death of a friend and after his subsequent interest in heart diseases, his condition deteriorated into a state of permanent anxiety and fear.

These emotional stimuli affected his autonomic nervous system and resulted in a variety of vasomotor symptoms, such as palpitation, extrasystoles, tachycardia, fluctuation of blood pressure, flushing of his face, dilation of his pupils, sweating, and cyanosis of the hands. While one was perfectly justified in regarding all

these manifestations as functional the patient became more and more inclined to regard them as certain proof of an existing and rapidly progressive cardiovascular disease. A vicious circle therefore developed and fear of imminent and sudden death was added to his anxiety state and aggravated his condition considerably.

It cannot be overlooked however that a few weeks before his death typical cardiac pain developed and became so severe that a status anginosus existed. This and the eventual fatal outcome will have to be explained by the rather sparse but not altogether negative autopsy findings. The localized small area of narrowing of the lumen of the descending branch of the left coronary artery caused by an equally small and localized but bulging atheromatous plaque in the absence of any significant sclerosis in the rest of the coronary tree must have caused a state of chronic coronary insufficiency which eventually led to his death. While under basal conditions the myocardium could apparently still be adequately perfused and oxygenated the patient's anxiety state with its subsequent imbalance of the vegetative nervous system impaired the normal compensatory adjusting mechanism of the heart and rendered the coronary circulation inadequate for the increased requirements of the myocardium. The coronary reserve seriously diminished and eventually became exhausted.

Whether or not superimposed coronary spasm also played a part during the spasmodic attacks of precordial pain is almost impossible to say. If one postulates inversion of T waves without RST segment deviations as the only pathognomonic electrocardiographic findings in coronary spasm as East and Oram believed and Evans more recently emphasized then coronary spasm could not be proved in this case. It must however be mentioned that all the tracings were taken after and none during an attack of pain. The fatal onset which awoke the patient from his sleep might have been provoked by an anxiety dream and terminated probably with ventricular fibrillation.

ACKNOWLEDGMENT The author wishes to thank Dr. William Evans for his generous help and cooperation.

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#### IMPLICATED 22 BILLION PACKS OF CIGARETTES

Some persons and groups have accepted the information now available on cigarette smoking and cancer of the lung as sufficiently convincing to implicate smoking as the major cause of the cancer and to justify proceeding with active campaigns to inform the public of the dangers of smoking (Such information as the U S Public Health Service has received to date did not prevent the 1957 sales of cigarettes from reaching an all time high of 22 billion packs) If smoking does cause cancer it is evident that such campaigns are a necessary responsibility of public health agencies In view of the numerous unresolved possibilities of bias in the case history population studies the conflicting epidemiological evidence and the inconclusive animal experimentation the evidence is still inadequate for moral certainty of the truth of the causal relation Investigation must continue and definitive interpretation should be postponed

—EDITORIAL

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p 537 Apr 1957

# Constitutional Hepatic Dysfunction in a Family

CHARLES M WEBER *Capt MC USA*

**W**HILE recognition of constitutional hepatic dysfunction apparently has little significance so far as its effect on the health of the individual is concerned its recognition is nonetheless important. Frequently confusion arises with hemolytic disease disease of the liver and disease of the biliary tract resulting in unnecessary restrictions on activities of the patient unnecessary surgical and medical procedures denial of insurance and dismissal from the armed services In brief recognition of the condition has such a strong negative value to the patient that greater awareness of the entity is highly desirable on the part of the physician

This report concerns a patient referred to our clinic for evaluation of jaundice Members of three generations were studied because intermittent jaundice had been observed

## CASE REPORT

A 21 year-old woman para 0 gravida 1 was referred from the obstetrical clinic to the internal medicine clinic of this hospital for evaluation of jaundice since birth The patient stated that she had had the usual childhood diseases with no complications or sequelae She denied any peritonsillitis or serious injuries

Both parents were living and well They both originated in Ireland and there was no history of jaundice from either Patient had had three siblings the first of which was a boy who had died at age six weeks as a result of pneumonia He was said to have been jaundiced The other two siblings were living and well The brother age 17 however also had had jaundice since early childhood

The patient did not smoke or drink any alcoholic beverage and she took no medication or drug of any kind

The review of system except for the present complaint was completely within normal limits

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The onset of the patient's jaundice condition dated back to several days after birth. She had been thoroughly examined at several institutions and later reassured that her chronic jaundice was of no clinical significance to her. Her only complaints over the years had been moderate fatigue and lassitude. She had never been anemic and there was no history of easy bruising, bleeding, or hemorrhages. There was no history of nausea, vomiting, abdominal pain, diarrhea, or fever. There had been no significant change in the color of the urine or in the stools in the past.

The routine physical examination findings other than scleral icterus and the tumor of pregnancy were perfectly normal. There was no evidence of any liver palms, spider angiomas, or enlarged liver or spleen.

The laboratory data revealed a red blood cell count of 5 000 000 per  $\mu$ l with a hemoglobin of 13 grams per 100 ml and a white blood cell count of 8 800 per  $\mu$ l with a normal differential. The blood morphology and urinalysis were within normal limits. The reticulocyte count was 0.7 per cent. The Coombs test, sickle cell preparation, and serologic test for syphilis were negative. The serum bilirubin was 5.4 mg per 100 ml, with 0.2 mg direct van den Bergh and 5.2 mg per 100 ml indirect van den Bergh. The total cholesterol, alkaline phosphatase, cephalin cholesterol flocculation, thymol turbidity, and sulfobromophthalein sodium tests were all normal. Urine and fecal urobilinogen studies were perfectly normal. Repeated laboratory studies consistently demonstrated an elevated serum bilirubin, only the indirect component being abnormal. The remainder of the studies remained normal. A liver biopsy demonstrated normal liver architecture (figs. 1, 2).

Total evaluation of the data presented led us to the conclusion that this represented a typical case of constitutional hepatic dysfunction.

Physical examination and some laboratory studies were made of the patient's parents, brother, and sister. The mother, who offered no history of intermittent jaundice, revealed a serum bilirubin of 1.4 mg per 100 ml, with 1.2 mg being indirect van den Bergh. The brother was found to be jaundiced but no other physical abnormalities were noted. His laboratory studies revealed a serum bilirubin of 14.1 mg per 100 ml, with a direct bilirubin of only 0.3 mg per 100 ml. Complete liver profile and hematologic work up were normal. Both the father and sister demonstrated no abnormality whatsoever.

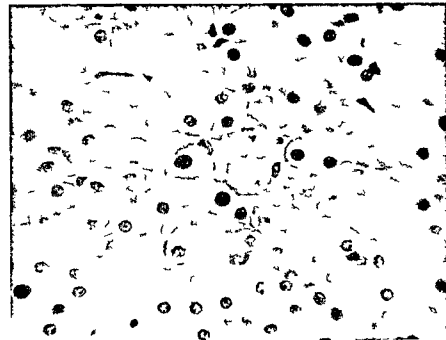
After the termination of the patient's pregnancy, physical and laboratory work up on her son revealed no abnormality. From the data collected, it appeared that there was a familial transmission of icterus on the maternal side of the family.

#### COMMENT

This condition was first described by Gilbert in 1901.<sup>1</sup> In his investigation into hemolytic jaundice, he encountered patients who exhibited a slight degree of bilirubinemia, but lacked all



Fig 1 Photomicrograph of inflammatory cells with mallob pattern (x 80)



F Hgb mg / l / / g 1 (x 344)

the other symptoms of the disease. He employed the term "cholemie simple familiale." Frequently today, Gilbert's name still remains identified with non hemolytic, non obstructive, acholuric jaundice of constitutional type, even though examples of mild hemolytic icterus, hepatic disease and carotinemia were probably included with his original cases.<sup>2</sup> Writers paid little attention to the condition in the next three decades. In 1935 Tozendaal, Comfort, and Snell<sup>3</sup> reviewed cases of jaundice with an "indirect" type of serum bilirubin. Of the cases, 48 showed no evidence of liver disease or hemolytic disease and they considered these patients to fall into the group of constitutional hepatic dysfunction. In 1941 Damoshek and Singer<sup>4</sup> reported two families with this type of jaundice, and coined the term "familial nonhemolytic jaundice." Comfort and Hoyne<sup>5</sup> in 1944 and Meulen gracht<sup>6</sup> in 1947 reported series of cases from their own practices.

According to Shay,<sup>7</sup> recent reports "suggest that the defect in bilirubin metabolism in constitutional hepatic dysfunction is caused, in part at least, by impaired activity of glucuronyl transferase, the enzyme responsible for the transfer of glucuronic acid from uridine diphosphoglucuronic acid to the bilirubin."

Constitutional hepatic dysfunction is characterized by chronic or intermittent jaundice which begins during youth or early adult life and lasts for many years. The clinical picture is fairly uniform. The jaundice is seldom intense but it often becomes deeper after intercurrent illness, exertion or fatigue. The patient remains in good health but frequently complains of fatigue, lassitude, dyspepsia, and symptoms of a functional type. Except for icterus, the results of the physical examination are essentially normal. The liver and spleen are not enlarged.

The most important laboratory finding, and of course a prerequisite in the diagnosis, is the bilirubinemia. Serum bilirubin levels are usually under 5 mg per 100 ml although values above 10 to 15 mg per 100 ml have been recorded.<sup>8</sup> The van den Bergh reaction is always of the "indirect variety." Examination of the urine is uniformly negative for bilirubin and increased amounts of urobilinogen. There are no abnormalities of the blood: the sedimentation rate is normal. There is absence of anemia, spherocytosis, reticulocytosis and normal red blood cell fragility, bone marrow, urobilinogen and feces.<sup>4</sup>

Normal values are obtained for liver function studies such as sulfobromophthalein sodium excretion, thymol turbidity and cephalin flocculation. The reaction to injected bilirubin is abnormal. Excretion is greatly delayed and the resultant retention of bilirubin three hours after injection is much greater than the high normal value of 15 mg per 100 ml.



Gallbladder function is usually normal as judged by cholecystography. Liver biopsy specimens have repeatedly revealed only essentially normal structure.

The etiologic mechanism for this entity appears to be a physiologic defect resulting in the impaired clearance of the serum bilirubin.<sup>1</sup> It is now recognized that direct van den Bergh is a glucuronic acid conjugated bilirubin. Inasmuch as in this condition there is a failure to form direct reacting bilirubin the most logical explanation in etiology would be a deficit or disturbance in the enzyme glucuronidase which is necessary for the formation of the conjugated bilirubin and thus producing a high threshold for bilirubin. The defect is said to be a dominant Mendelian trait which may be carried by either sex. The fact that several members of the family may be affected is well documented.<sup>2</sup>

The diagnosis of constitutional hepatic dysfunction is made primarily on the basis of exclusion. The elevations of concentration of bilirubin giving the indirect van den Bergh must be distinguished from those of hemolytic jaundice, chronic hepatic disease and those persisting after acute hepatic disease. The exclusion of obstructed jaundice and hepatocellular disease by the usual studies and of a subtle hemolytic process by reticulocyte counts and quantitative fecal urobilinogen suggest the diagnosis. A normal liver biopsy gives final histological confirmation.

The variety of this disease as described by Dubin and Sprinz should also be kept in mind. However here there is an elevation of a direct as well as an indirect type of bilirubin, the presence of dark urine and bilirubinuria, some impairment of liver function studies and nonvisualization of the gallbladder on cholecystography. The liver exhibits normal structure but is grossly and histologically discolored by the presence of a coarse brown pigment in the parenchymal cells.

On the basis of long term follow up studies the prognosis is generally said to be excellent. This condition does not predispose to any chronic hepatic disease.

Actually satisfactory treatment has not been devised and it is indeed questionable whether any treatment is indicated if the condition does not affect the health of the individual. Steroid therapy was used in an attempt to reduce the hyperbilirubinemia without satisfactory success.

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### USE OF AMPHETAMINE BY ATHLETES

the athlete who will use amphetamine is a problem in mental health as well as a potential problem in physical health. It may be said by some that since too great a valuation is placed upon the ability to break records of all kinds with a faster mile, broader jump and higher vault the athlete is under too great popular pressure. Like the paratrooper he may be held to be entitled to reach for a stimulant. However to equate the long distance runner in time of peace with the soldier in time of war betrays major loss of perspective. The soldier has his life at stake and the lives of many others. For the disciplined runner the very qualities that make for self-discipline and superior performance are those that should prevent him from taking amphetamine to achieve success. If objective evidence should at any time indicate that stimulant drugs are sometimes being used the very least of the physician's responsibilities would be to publish the evidence so that watch can be kept for harmful manifestations when they make an appearance in the years to come.

—EDITORIAL

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 P 1195 Dec 12 1957

# Left Sided Traumatic Diaphragmatic Hernia Involving Solid Viscera

C WILLIAM ROGERS L t ant MC USN

**T**HE first account of a diaphragmatic hernia was written by Ambrose Pare in reporting the case of a military officer who died in great pain following a penetrating chest wound. Postmortem examination disclosed the presence of abdominal viscera in the chest. Very little consideration was given to such hernias until World War I when shrapnel and bayonet wounds of the chest and upper abdomen were common and many cases of traumatic hernia were seen.

The advent of the roentgen ray was followed by the incidental discovery of diaphragmatic hernias in many patients in whom the condition undoubtedly would have remained undiagnosed unless they came to autopsy. Giffin reviewed the literature in 1912 and found that only about 2 per cent of some 600 reported cases of diaphragmatic hernia were correctly diagnosed before death.

Many classifications have been proposed but Harrington simply divides all diaphragmatic hernias into traumatic and non-traumatic varieties. Traumatic hernias may result from direct or indirect injury to the diaphragm or from inflammatory necrosis of the diaphragm. The following case is one in which a diaphragmatic hernia presumably caused by minor trauma, presented a confusing diagnostic problem because of the herniation of solid viscera.

## CASE REPORT

The patient was a 49 year-old man who related that he had experienced a tearing sensation with pain in the lower part of his chest on the left side after taking a healthy swing with a golf club on 25 February 1957. A roentgenogram of the chest taken on 27 February revealed what appeared to be a mass in the left lower lung field. A thoracentesis performed at another hospital yielded 8 ml of bloody fluid.

The patient was transferred to this hospital on 25 March with a diagnosis of cystic tumor of left lung for further diagnostic studies and appropriate treatment. On admission he was entirely asymptomatic.

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Physical and laboratory examinations were essentially negative and a bronchoscopy with biopsy failed to aid in diagnosis.

Roentgenograms of the chest taken on 10 April (fig. 1) showed soft tissue density with reactive changes in the left lower lung field. A thoracotomy was performed on 11 April with preoperative diagnosis of "undetermined lung tumor," and the spleen and a large mass of omentum were found in the left thorax, entering through a posterolateral defect in the left diaphragm. The spleen was removed, the omentum was replaced in the peritoneal cavity, and the diaphragmatic defect was repaired.

The patient was discharged from the hospital on 28 April following an uneventful recovery.



Figure 1 This examination was performed 44 days after the patient experienced pain in the left lower chest while swinging a golf club. The soft tissue density in the left lower lung field consists of spleen and omentum, and simulates an intrathoracic tumor. Note the reactive changes about the density in the PA projection.

#### DISCUSSION

When a hollow viscus is herniated through the diaphragm, the diagnosis usually is easy because of the history of trauma and the occasional presence of an air-containing organ above the normal diaphragmatic level. The use of gastrointestinal contrast studies usually will resolve any doubts in this type of hernia. It must be remembered, however, that a diaphragmatic hernia may occur many years after the traumatic incident.<sup>4-6</sup>

The present case is of interest because of the insignificant amount of the trauma that produced the herniation, and also because one expects to find a hollow viscus herniating, when

the diaphragmatic rupture occurs on the left. A number of reports have appeared in recent English literature of cases of liver herniation on the right without accompanying hollow organs but few cases of solid herniations on the left have been seen. Hughes and associates reported a series of 28 traumatic diaphragmatic hernias of which 23 were on the left and 3 involved only solid viscera. Incidentally these three patients remained undiagnosed until thoracotomy.

If the clinician or radiologist suspects a diaphragmatic hernia, diagnostic pneumoperitoneum may be of great value in making a positive diagnosis and in averting a diagnostic thoracotomy. Clay and Hanlon presented four cases of solid visceral herniation through the diaphragm that were diagnosed with pneumoperitoneum without resorting to a diagnostic thoracotomy. They mentioned no history of trauma to any of the four patients but as illustrated in the case presented here, the traumatic incident may be relatively insignificant and in some cases may only be mentioned on careful questioning.

The roentgenologic appearance of these lesions can be confusing because of the presence of fluid adjacent to the mass in the chest. Thoracentesis may yield bloody, foul smelling fluid<sup>1</sup> and it is conceivable that puncture of the hernial contents could occur during the procedure, adding further importance to the urgency of establishing a correct diagnosis.

### SUMMARY AND CONCLUSIONS

A case of solid visceral herniation through the left diaphragm following minimal trauma was only diagnosed at thoracotomy for suspected lung tumor. Such herniation of solid viscera on the left side is more confusing than that on the right because one expects to find stomach, colon, or small bowel either accompanying the solid viscus or comprising the hernial contents exclusively. Although not utilized in this case, diagnostic pneumoperitoneum usually will result in a definitive diagnosis. The physician should consider the possibility of a diaphragmatic herniation in any patient whose chest roentgenogram displays a density adjacent to the diaphragm.

ACKNOWLEDGMENT: The authors are grateful to Captain Robert B. W. MCUSN, first lieutenant, for his help in the preparation of this paper and to Dr. B. G. H. Ford, Surgeon, for his help in the preparation of this paper.

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—INVENTION IS MADE BY THE ARMED FORCES,  
in Mission Design & Development  
p. 22 Dec 1957

# Juvenile Fibromatosis

THEODORE R. WAUGH, Captain USAF (MC)

THE classification of fibrous tissue tumors has been confused in the past by the large number of specialists who described conditions arising within their own fields. In 1954 a significant contribution was made by Stout<sup>2</sup> toward the organization of this subject in order to have some framework on which to base a prognosis and evaluate treatment. The juvenile fibromatoses include three more common types: (1) desmoid fibromatoses, the scar like tissue such as is found in the torticollis of infants; (2) differentiated fibrosarcomas, or those which do not usually metastasize; and (3) fibromatoses, those fibrous growths which cannot be listed elsewhere. In addition, there are five other types: plantar and palmar fibromatoses such as Dupuytren's, juvenile aponeurotic fibroma, keloid fibromatosis, diffuse muscular fibromatosis, and generalized fibromatosis, the multinodular congenital fibrosarcoma.<sup>3</sup> The separation of these tumors in children from birth to 15 years is arbitrary, however, there is evidence that some of the fibromatoses may be congenital, somewhat less than half of reported cases, particularly the desmoid type, manifesting themselves in infancy. Certainly the fibrous tissue growth potential is altered in children.

The role of trauma and estrogenic imbalance are considered in certain cases to be of etiologic significance, but a correlation is more frequently absent than present.<sup>7</sup>

The following is a case of juvenile fibromatosis with keloid formation in the excision scar.

## CASE REPORT

A 16-month-old Caucasian boy had a history of a gradually increasing mass in the lower right lateral thigh since the age of 3 or 4 months. It was the opinion of the mother that in the past 3 months the mass had been increasing more rapidly in size. There was no suggestion of antecedent trauma.

Pat History: The patient was born of a normal full term pregnancy with spontaneous delivery in cephalic presentation. There was one other sibling, a 4-year-old male. In the neonatal period there were no

convulsions hemorrhages, cyanosis or jaundice noted. The child's development and nutrition were normal.

**Physical Examination.** The examination was normal in all respects with the exception of a hard relatively immobile mass on the lateral aspect of the lower right thigh which measured approximately 6 cm in its greatest diameter. There was no unilateral adenopathy.

**Laboratory Studies.** Hemogram prior to admission revealed a leukocyte count of 5050 per  $\mu$ l with a differential count of 12 per cent neutrophils and 88 per cent lymphocytes. The hemoglobin was 11.8 grams per 100 ml. The bleeding and coagulation times were normal. On hospital admission the leukocyte count was 6500 per  $\mu$ l with a differential count of 8 per cent neutrophils, 88 per cent lymphocytes, 3 per cent monocytes and 1 per cent eosinophils. Hemoglobin was 10.8 grams per 100 ml. Urinalysis was normal.

Radiologic examination prior to hospitalization revealed the presence of a soft tissue mass in the right lower lateral thigh. This mass was considered to be independent of the periosteum of the femur. There was no calcification.

**Course in Hospital.** On the day after admission under general anesthesia the tumor mass of the right vastus lateralis muscle was exposed. This was estimated to measure 6 by 4 by 2 cm. Because of the absence of encapsulation with infiltration into the surrounding muscle biopsy alone was performed without any attempt to remove the tumor. The specimen was yellow white in color and firm in consistency. It was sent for pathologic examination and reported by different examiners as desmoid tumor and reactive fibrosis. Neither pathologist believed there was any evidence of sarcoma (figs 1 and 2).

Consequently under tourniquet the previous biopsy site with the adjacent tumor tissue was excised from the right vastus lateralis muscle removing a surrounding zone of normal muscle adjacent tendon the periosteum of the femur and the lateral suprapatellar pouch of the knee. Repair was effected by closure of the suprapatellar bursa reapproximation of the muscle and tendon. The lower extremity was immobilized in a posterior splint with the knee in extension. The patient's postoperative course was uncomplicated and on the 14th hospital day he was discharged in a high leg-cast. In three weeks the cast was removed and the incision was well healed.

At the five month follow up visit the child had regained completely normal knee function and there was no evidence of recurrence at the site of the operation or of the development of tumors in other areas. However the surgical scar showed some definite keloid development.

**Pathologic Findings.** Grossly the tumor measured 6 by 4 by 2 cm. It was yellow white in color and of firm fibrous like consistency. There was noted an indefinite line of demarcation from the surrounding muscle tissue. Microscopically there was a poorly circumscribed mass of





Fig. 1 Photomicrograph of fibromatous tissue (H&E, 200x)

relatively cellular fibrous tissue with slender fibroblasts. There were occasional groups of uniform, lightly hyperchromatic fibroblasts resembling those in the fibrous stroma. Mitotic activity was not noted. Within the tumor tissue were some degenerated muscle fibers with essentially normal nuclei adjacent to the tumor tissue. The microscopic picture was one of a juvenile fibromatosis.

#### DISCUSSION

The juvenile fibromatoses represent an important category of fibrous tissue tumors because of their insidiously progressive growth characteristics. While locally invasive and possibly crippling, they rarely metastasize.

With this rationale, the present treatment is one of radical local excision where this can feasibly be performed. — Stout



Figure 2 Photomicrograph of section from the biopsy specimen showing infiltration into muscle ( $\times 50$ )

noted that some fibromatoses became quiescent after mere biopsy and he suggested that the plantar fibromatoses and the diffuse muscular fibromatoses should be left untreated. However, the tendency to local recurrence is particularly strong in the major groups<sup>4,7</sup> and this may necessitate repeated local excisions, which in the extremities is preferable to amputation.

The development of a keloid in the surgical scar represents an interesting association within the fibromatoses and is suggestive of common causative factors.

#### SUMMARY

A case of juvenile fibromatosis has been presented with the gross and microscopic pathologic findings. This was treated by wide surgical excision of the tumor. The characteristic behavior

of infiltration and tendency to local recurrence but not metastasis is the basis for the surgical treatment of these lesions. The development of a leioid, another type of fibrous growth within the juvenile fibromatoses following excision of the original tumor is an unusual occurrence.

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## TREATMENT OF ACNE

Acne vulgaris, the blemish of youth, is a blemish of disease. It is the most common skin condition, resistant to treatment, aesthetically unpleasant, and demoralizing. With a complete pathology and pathogenesis. No specific treatment is known. Good health habits, a local antiseptic, and the basis of treatment. The efficacy of adotherapy is undeniable. In a series of 107 patients, the administration of multivitamin preparations in high dosage, with thyroid extract and antihistamines, both in small doses, has given excellent results in 56 percent of cases, and satisfactory results in 90 percent. This therapy, on account of its simplicity, has many advantages and efficiency constitutes a treatment of choice in acne vulgaris.

—PAUL POIRIER, M.D.

in *C. d. M. d. l. A. t. J. u r n a l*  
pp 869 870 N 1 1957

# Ureteral Ectopia

ANTHONY A BORSKI Major MC USA  
ROBERT W PARSONS Captain MC USA

**W**E believe that there is a widespread lack of awareness of ureteral ectopia. This is borne out by the fact that 26 different physicians treated a young girl during a seven year-period without suspecting this congenital condition as a cause of her repeated illnesses.

## CASE REPORT

An 11 year-old girl was admitted to this hospital on 16 October 1954 for urologic work up for urinary incontinence. The history as obtained from the parents dated the child's difficulties for approximately 7 years. At age 3 the child had intermittent low-grade fevers associated with dysuria, and her underclothing and bed were almost always wet. In addition there was a yellowish vaginal discharge. She was treated with various medications with some improvement. However she continued wetting her underclothing almost continuously. After 5 years of treatment with medications and after having been treated by a dozen different physicians for the urinary incontinence it was suggested that psychiatric treatment should be used in order to help control the symptoms. After a course of psychiatric treatment there was no improvement and the mother continued to seek medical aid for this distressing problem in this young child. Different physicians were consulted again and vaginal douches and suppositories were used along with antibiotic therapy. After seven years of frustrating effort the 27th physician suggested a urologic investigation. This child had never previously had a urologic work up. One physician even had suggested psychiatric treatment for the mother because of her insistence that this was not an emotional problem as she believed that she knew her daughter better than the physicians.

Physical examination was essentially normal except for inflammation and lichenification over the genitalia and inner thighs from urinary leakage.

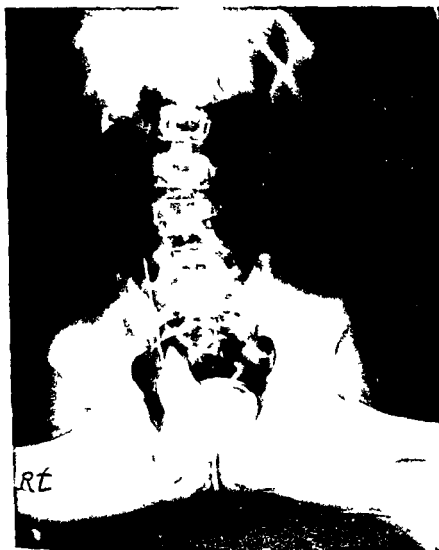
Urinalysis, complete blood cell count and blood urea nitrogen were all normal. A tuberculin skin test using PPD was negative in 48 hours. Roentgenographic findings of the chest were normal. Intravenous pyelograms showed a reduplication of the right kidney and a normal left kidney (fig 1).

On 22 October under Penthal (brand of thiopental sodium) anesthesia a cystoscopy was performed, and this showed a normal bladder with a single orifice on the right and a normal left orifice. During this examination a catheter was passed up the lower right kidney which



Fig 1. Intravenous cystogram. The arrow points to the upper segment of the dilated kidney of the right. The left kidney normal.

was normal. A vaginal examination revealed an ectopic ureteral orifice in the anterior vagina. A catheter was introduced through the vagina into this ectopic orifice and it became coiled in a dilated tortuous ureter (fig 2). On 25 October small upper kidney and markedly dilated tortuous ureter were removed. The lower kidney was normal. Postoperatively there was no further urinary dribbling or discharge from the vagina. A 6-month follow-up revealed a normal intravenous urogram and a healthy asymptomatic child and mother.



*Fig. 2 Retrograde pyelogram. The catheter through the bladder shows a normal ureter. A catheter through the vaginal ectopic orifice is coded in the tortuously dilated aberrant ureter.*

#### DISCUSSION

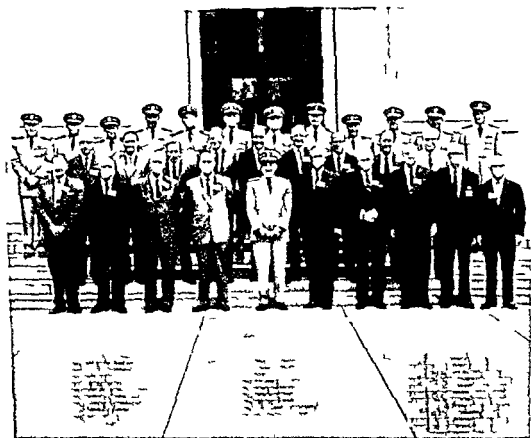
Ureteral ectopia is no longer considered a rare entity. It is being recognized clinically with increasing frequency. A review of the literature by Burford, Glenn, and Burford<sup>1</sup> in 1949 showed that 425 cases had been reported since the review of Givinto in 1813, and each of the past 9 years has seen a number of new cases reported. In autopsies in children the incidence of ureteral ectopia is reported to be 1 in 1 600 and is found from three to four times as frequently in females as in males.<sup>2</sup> However, as illustrated by our case, there is still a widespread lack of awareness of this diagnostic possibility.

The embryologic background was well described by Hepler<sup>3</sup> and by Wesson. The ectopic orifice most commonly drains a reduplicated ureter, and in 75 per cent of the cases it is the



## NAVY MEDICAL RESERVE CONSULTANTS BOARD DISCUSSES GRADUATE TRAINING PROGRAM

The Reserve Consultants Board of the Bureau of Medicine and Surgery recently met at the National Naval Medical Center Bethesda Maryland to discuss the Navy's Graduate Medical Training Program with the Surgeon General Rear Admiral Bartholomew W Hogan MC USN and his staff. Each member of the Board represents one of the medical specialties and the majority hold teaching positions in medical schools throughout the country. The Honorable Frank B Berry M D Assistant Secretary of Defense (Health and Medical) was a guest at the meeting.



The Navy's Graduate Medical Training Program was planned and instituted at the close of World War II by several of the members of the Board who were senior officers in the U S Naval Reserve on active duty at that time. Since their release from active duty they have continued their interest in the Navy and have given freely of their time and advice visiting the Navy's medical facilities at the request of the Surgeon General to review the training programs. The high standards of the training have produced well qualified naval medical officers who in turn provide better patient care. The program has been a very important feature of the professional career pattern of the Navy.



# A MESSAGE FROM THE A M A

The American Medical Association has always been keenly interested in and since World War II particularly active concerning the medical care furnished our military personnel. Opportunities for study, research, actual treatment of patients, rotation of medical assignments, and assignment of medical personnel to nonmedical duties also are matters of concern to the Association. The development of a strong and attractive medical service staffed for the most part by qualified career officers in the Armed Forces, Veterans Administration, and Public Health Service is in the Association's view in the best interest of the public welfare. The development of such services depends on the confidence and intimate collaboration of the medical profession of the nation.

Since the creation of its Council on National Defense in 1946, the Association has been in particularly close and constant contact with the complex problems of military medicine. The best medical care for our servicemen must be provided in a manner that is economical and yet consistent with the health needs of our civilian population. To accomplish this, the Association has consistently advocated that the military medical services be strengthened by legislation and administrative action which would attract and retain well qualified physicians in numbers sufficient to meet the needs of the military services.

One effort toward this accomplishment is to offer to such qualified physicians a pay scale at least as attractive as that offered by other Federal medical services. In other words, the Association believes that the Armed Forces must be in a position at least equal to that of other Federal agencies if it is to attract and retain medical personnel who will render the highest medical service.

The Medical and Dental Officer Career Incentive Act of 1956 had the unreserved support of the American Medical Association. Witnesses for the Association appeared before the committees of Congress which considered this legislation. This Act is a valuable method of preserving and improving the quality of military medical manpower. This legislation provides special pay of \$100 per month which increases in three increments of \$50 each at 2, 6, and 10 years of active service as a medical officer for a total special pay of \$250. Thus the career medical officer is recompensed for his personal expenses, tuition, et cetera, in securing his premedical and medical education to a degree commensurate with line officers who attended the military or naval academies. Such step up salary increases appeal to

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experienced officers, many of whom had intended to abandon military careers for the private practice of medicine. The result of this legislation has been salutary. The increase in special pay has had the effect of slowing down the resignation rate of regular military medical officers, of increasing the procurement of new officers, and of providing stability in the medical corps.

The benefits achieved by military medicine under the Medical and Dental Officer Career Incentive Act of 1956 were threatened during the legislative process which culminated in the enactment of Public Law 85 422, approved May 20, 1958, which adjusts the method of computing basic pay for officers and enlisted members of the uniformed services. It was proposed that the special pay received by medical officers of the Armed Forces be reduced by as much as \$100 to \$150 monthly in the groups of the most experienced physicians. True, the proposed reduction would not have resulted in decreased compensation for any medical officer but, nevertheless, the proposal undoubtedly would have had an adverse effect on the attraction and retention of qualified physicians for the military services. For this reason, the Association in vigorous opposition to the proposed reduction for medical officers made its views known to the Congress.

It was and is, the Association's view that the special pay provisions of the Medical and Dental Officer Career Incentive Act of 1956 is largely a method of equalizing earnings to compensate for the long and expensive medical education and the resultant delay in earnings of the medical doctor.

It is gratifying that the Association's position was accepted by Congress and thus prevailed in this matter. The recently enacted Public Law 85 422 did not alter the incentive pay provisions of the Medical and Dental Officer Career Incentive Act of 1956.

The military medical officer may be certain that the American Medical Association, through its Council on National Defense, will continue to support legislative proposals that contribute to the desired goal of a stable career medical corps which is essential if the members of the U. S. Military Forces are to receive medical care that is second to none.

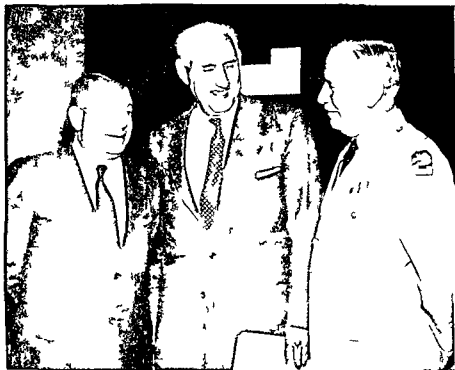
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## World Congress of Aviation Medicine

Brigadier General M. S. White, USAF (MC), president of the Aero Medical Association, will officially represent the society and the Surgeon General of the Air Force at the World Congress of Aviation Medicine in Louvain, Belgium, 23-27 September.

## SECOND ARMY CONSULTANTS AND HOSPITAL COMMANDERS MEET AT FORT GEORGE MEADE

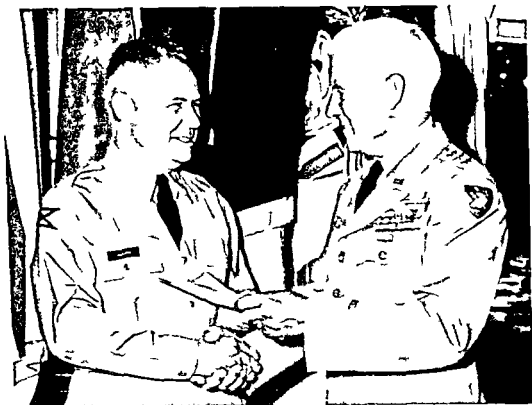
A conference of civilian medical consultants and hospital commanders of the Second United States Army was held at Fort George G Meade Maryland on 28-29 May 1958 under the direction of Colonel Francis P Kintz MC USA Second Army Surgeon The U S Army Hospital Fort Meade under the command of Colonel Charles S Mudgett MC USA was the host facility.



Dr. Rad and Gittman with Col. Kintz.

The purpose of the conference was to further the professional relationships between civilian medical consultants and Second Army hospital commanders to evaluate and discuss recent advances in medical procedure technique and drugs and to appraise the professional standards of medical care within the Army's treatment facilities. In addition to the hospital commanders who attended distinguished guests included Major General I S Ravdin MC USA (Ret) Chairman Second Army Civilian Consultants Advisory Committee Colonel Douglas B Kendrick MC USA Chief Surgical Consultant Department of the Army Dr Melford S Guttmacher Chief Medical Officer of the Supreme Bench of Baltimore Maryland and Dr M R Hillman Director of Virus Research Merck Sharpe & Dohme Research Laboratories.

## WEST POINT HOSPITAL GIVEN ACCREDITATION



The West Point Army Hospital recently was granted accreditation by the Joint Commission of Accreditation of Hospitals. Lieutenant General Garrison H. Davidson USA (right) Superintendent of the United States Military Academy is shown presenting the announcement of the accreditation to Colonel James B. Stapleton MC USA Hospital Commander.

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### Official Decorations

The following awards were recently announced by the Department of the Army

#### Legion of Merit

R b r t T G r Col MC USA

#### Commendation Ribbon

E th Cl n Lt C I ANC USA

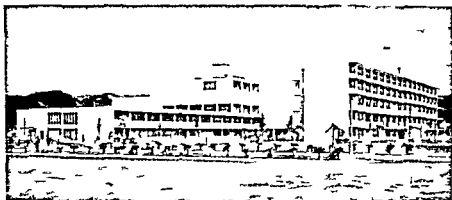
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## Army Dedicates New Hospital on Okinawa

Lieutenant General James E. Moore USA, High Commissioner of the Ryukyu Islands, was the principal speaker at the dedication recently of a new 250-bed Army hospital on Okinawa. Many distinguished visitors stationed in the Far East attended the ceremonies for the only military hospital in the Islands when host for the occasion was Colonel James T. McGibony MC USA, Commander of the new hospital and Surgeon, U.S. Army Ryukyu Islands.



*New U.S. Army Hospital Ryukyu Islands*

The construction of the hospital began in December 1954 and many obstacles were encountered by the engineers before its completion. The building is partly air conditioned and contains oxygen and master clock systems, vacuum installations for the operating and delivery rooms, and an elapsed time system in the surgery. Staffed by Army medical personnel, the new hospital offers its services to all U.S. military units in the Islands.

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## Captain Gorby Receives Hoff Medal

Captain Earl W. Gorby MC USA, son of Major General Alvin L. Gorby MC USA, Chief Surgeon, U.S. Army Europe, was the 1958 recipient of the Hoff Medal, awarded annually to the student with the highest proficiency in the Military Medicine and Allied Sciences Course of the Walter Reed Army Institute of Research. Established in 1897 in memory of Colonel Alexander H. Hoff, the medal formerly was given each year to the outstanding graduate of the Army Medical School. Graduation ceremonies of the nine-month course were held on 20 June.

# OFFICERS CERTIFIED BY SPECIALTY BOARDS

## Supplementary Listing

The Surgeons General of the military departments have announced certification by specialty boards of the following officers of the regular establishment since publication of listings in previous issues of the *Journal*

### American Board of Radiology

Edw rd A Sheldon Capt USAF

M tth w F J Yenney Jr Lt USN

### American Board of Obstetrics and Gynecology

R bert C Drip Lt C mdr USN

Hal dan G A Faaland Comdr USN

Str iton R E st r M J USAF

M ble A Frew Lt USN

### American Board of Internal Medicine

R b rt E D F r st Lt USN

Thom s W Sh eh y C pt USA

M x E Musgrav Lt Comd USN

J m L Spencer C pt USN

### American Board of Surgery

Harry C Gr e Jr Lt C l USAF

### Board of Thoracic Surgery

B lli G Str te Lt C l USAF

### American Board of Anesthesiology

R bert J McC Maj USAF

### American Board of Preventive Medicine

#### *Public Health*

H ry J D nn lly M J USA

Alot P cze k Maj USA

#### *Aviation Medicine*

Charl N M s Lt C l USAF

L wre c T Od l nd M J USAF

H ry C. Mor t Jr M J USAF

#### *Occupational Medicine*

J hn A P t o M J USAF

### American Board of Oral Surgery

Joh P Jar b k C pt USN

Jer m C St p k Capt USN

### American Board of Periodontology

P t r C F di Lt Comdr USN

### American Board of Veterinary Public Health

J eph D M g s Col USA

## Dr Youmans Named Medical Research Advisor

Dr John B Youmans dean of Vanderbilt University Medical School has been appointed Technical Director of Research for the Surgeon General of the Army effective 1 September 1958. He is resigning his position at Vanderbilt where he has served since 1950 to move to Washington. A retired colonel of the Army Medical Corps, Dr Youmans served during World War II in the CBI Pacific and European Theaters and was awarded the Legion of Merit and the French Legion of Honor. He will serve as principal advisor to the Surgeon General and his staff in all scientific and technical matters related to medical research and development.



Dr. Youmans

Dr Youmans is now serving as consultant to the Army Surgeon General's Preventive Medicine Division and to the Interdepartmental Committee on Nutrition for National Defense. He is a member of the Assistant Secretary of Defense's Panel on Military Medicine and the National Research Council Committee for the Quartermaster Subcommittee on Nutrition.

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## Col Snyder Heads Physical Therapists

Lt Col Agnes P. Snyder, Assistant Chief of the Army Medical Specialist Corps and Chief of the Physical Therapist Section, recently was elected president of the American Physical Therapy Association for a three-year term to the 1958 convention of the organization at Seattle, Washington. She is the retiring Speaker of the House of Delegates of the Association. Colonel Snyder, who is a native of St. Mary, West Virginia, is a graduate of Marshall College, Huntington, West Virginia, and has completed a physical therapy course conducted by the Army Medical Service at Walter Reed Army Hospital, Washington, D.C., and holds a master's degree in physical therapy from the Medical College of Virginia. She entered the Army service in 1933.



Col. Snyder

## DEATHS

CANADA Joseph Clayton Lieutenant Colonel MC USAR of Tahlequah Okla stationed at Ft Bragg N C graduated in 1929 from the University of Oklahoma School of Medicine Oklahoma City Okla commissioned a lieutenant colonel in the United States Army Reserve 28 May 1953 ordered to active duty 5 July 1953 died 14 June 1958 age 54 at Walter Reed Army Hospital Washington D C of a heart attack

COX Ardis Tillman Lieutenant Colonel MSC USA of Long Beach Calif stationed at William Beaumont Army Hospital El Paso Tex graduated in 1932 from the University of New Mexico Albuquerque N M commissioned a first lieutenant in the Army of the United States and ordered to active duty 12 August 1943 died 28 May 1958 age 48 at El Paso of myocardial infarction

MANN Joseph Lee Lieutenant Colonel USAF (MC) of Hampton Va commander of the U S Air Force Hospital Griffiss Air Force Base New York graduated in 1938 from the University of Virginia Department of Medicine Charlottesville Va commissioned a first lieutenant in the Army of the United States 26 April 1947 ordered to active duty 11 May 1942 ordered to inactive duty 2 January 1946 transferred to the United States Air Force Reserve and ordered to active duty 10 January 1949 commissioned a captain in the United States Air Force 10 August 1950 died 19 March 1958 age 43 at the U S Air Force Hospital Langley Air Force Base Virginia of myocardial infarction

MARCANTONI Charles Louis Lieutenant DC USN of Jackson Heights N Y stationed at the Naval Communication Facility Port Lyautey Morocco graduated in 1957 from the Georgetown University School of Dentistry Washington D C appointed a lieutenant in the United States Naval Reserve 1 July 1957 ordered to active duty 15 July 1957 appointed a lieutenant in the United States Navy 27 May 1958 died 15 June 1958 age 28 at Mehdia Beach near Port Lyautey of drowning

THAYER James Manning Jr Captain USAF (MC) of Memphis Tenn stationed at the U S Air Force Hospital Landstuhl Germany graduated in 1954 from the University of Tennessee College of Medicine Memphis Tenn commissioned a first lieutenant in the United States Air Force Reserve in 1955 ordered to active duty 24 February 1955 died 15 February 1958 age 27 at Mount Vesuvius near Naples Italy in a military aircraft accident

THOMPSON Henry Aubrey Lieutenant Commander MSC USN of Willisville Ark stationed at the U S Naval Hospital Guantanamo Bay Cuba enlisted in the United States Navy 8 October 1931 and served in an enlisted status until 15 May 1943 appointed a warrant officer in the United States Navy 15 May 1943 promoted ensign (HC) in the United States Navy 15 July 1944 died 28 May 1958 age 45 at the U S Naval Hospital Guantanamo Bay Cuba of a heart attack

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## Army Chemical Corps Develops New Mask

The Army Chemical Corps has announced the development of a new type of oronasal air filtering mask that is said to be 10 to 15 times more effective in filtering out airborne bacteria than the conventional surgical mask. It will be used in testing the efficiency of experimental warfare protective masks.



## Reviews of Recent Books

THE CHEMISTRY AND CHEMOTHERAPY OF TUBERCULOSIS A mp l t  
and t l w f g k w l d g n th h m try f t b l  
b ll d th prod h m al hang d p h  
h d h m l asp f th tr m t f b l by E mond  
R L g M D Ph D S D 3d d 450 p g ll st t d Th  
W ll m & W lk C mpa y B ltim Md 1958 P \$12

This book by an internationally known and leading authority on tuberculosis is a compilation and critical review of existing knowledge on the chemistry of tubercle bacilli and their products, chemical changes and processes in the host and chemical aspects of the treatment of tuberculosis. The author attempted to correlate the subject matter in such a way as to make the mechanism of action of antituberculous drug more clearly understood. The chemical aspects of tuberculosis are so varied and complex that a summation of the known facts concerning tuberculous persons and the chemistry of tubercle bacilli should be helpful to the research worker and specialist seeking to find improved methods of treatment of this insidious disease. The practical information on chemotherapy of tuberculosis makes this volume a very desirable reference for our medical libraries.

—CARL W. TEMPEL Brig Gen, MC USA

PHYSICAL METHODS IN PHYSIOLOGY by W T C H M Sc 375 p g  
ll tr d Ph l ph l l b ry l N w Y k N Y 1957 Pn \$10

In no sense is this a textbook of physiology; it is instead a compact and well-written volume on physiological methodology discussing for the most part the techniques unavailable to the medical student during his practical training. Mathematical formulae are extensive and a theoretical basis for described measurements is usually presented. With this emphasis there is minimal discussion of data and even less on correlation.

A might be expected to be coverage given to muscle nerve and the circulatory system, the indirect approach to endocrinology, digestion. A concise but helpful citation of relevant literature is included.

Though conspicuously short rather than *Glass's Medical Physiology*, this text should be of value to the physiologist or to the research worker concerned with physiological methodology. While modern movements are referred to, physiological basis we have not yet reached the stage where this volume will be of interest to the clinician.

—ROBERT D. DRUYAN Lt MC USNR

THE STORY BEHIND THE WORD S m l t g O g n f M d l T ms  
by H rry W M. D 342 p g Charl C Th m Sp ngf ld Ill  
1958 P \$8 50

This alphabetical compilation of more than 5700 words with brief statement of the origin and history of each term. Also included are brief biographies of great personalities of medicine. While the

author a physician states in his introduction that these are medical terms and that his concern is with medical etymology there are a great number that appear to have little meaning within the medical frame of reference For example one wonders about the inclusion of such words as climate geography blockhead idea cynic, oyster watershed pen jerry built and biscuit

*The Story Behind the Word* is interesting but it falls somewhat short of the claims of the author who calls it a "veritable treasure house of linguistic adventure which gives medical terms "a newer and fuller meaning Perhaps the answer lies in his further statement that the project was undertaken as a hobby and involved painstaking research over a 10 year period—which obviously culminated in some 5 700 terms now published in a volume One believes that either the volume should have been edited more systematically to include only medical terms or else not described as a reference work on medical etymology The casual reader will find the style witty and the reading interesting but the volume is a luxury item for the library it cannot be considered a basic reference —MAE M LINA Ph D.

THE ESSENCE OF SURGERY by C Stuart Welch M S M D Ph D and Samuel R P uers Jr A B M D M Sc D 320 pages illustrated W B Saunders Co Philadelphia Pa 1958 Price \$7

This is a concise and engaging treatise on the basic principles and foundations of present surgical practice After a short historical review which sets the stage for the basic concepts which follow the authors have proposed that the surgeon's entire area of practice can be categorized into three types of injuries They are loss of body tissue (wounds) loss of body fluids and infection The development of their thesis on these broad concepts is logical lucid and comprehensive despite the small size of this volume The philosophic approach of the authors truly expresses the essence of surgery The broadening experience resulting from perusal of this volume is extremely gratifying and is recommended particularly to the younger man beginning his surgical training Here he may consciously view early in his career the foundations of a discipline which will engage his entire lifework For the trained surgeon this volume will integrate many isolated surgical experiences into a composite orderly structure worthy of much thoughtful contemplation I believe the authors have been unusually successful in presenting their thesis This volume is highly recommended for the surgeon's bookshelf

—DAVID GOLD Col USAF (MC)

HANDBOOK OF TREATMENT OF ACUTE POISONING by E H Bensley M B E B A M D F A C P and G E Joron B A M D C M F A C P 2d edition 212 pages Published by E & S Livingston Ltd Edinburgh and London 1958 The Williams and Wilkins Company Baltimore Md exclusive U S agents Price \$4

This small concise book is presented as a quickly available specific guide to the immediate treatment of acute poisonings It is not intended to be a textbook of toxicology The book is small enough

to be carried easily in a physic an s bag or even a coat pocket and probably would best serve its purpose by being accessible for quick perusal when needed

The book is div ded into two ections the fir t devoted to principles of treatment this is a good review of the subject The second section d ls more sp cific lly with various types of poisons Recommended tre tment in each instance includes measures to be used both before and fter the arriv l of the physician

The book fulfills its stated purpose very well and should be of special v lue to house off c rs and phy cians engaged in general p actice —HARVEY F REITZ *Capt. (MC) USN*

OBJECTIVE APPROACHES TO TREATMENT IN PSYCHIATRY by L  
Al d M D Am n L t S P bl t N 327 M o-  
g ph Am L c Obj t P y h try d t d by W  
H l y G tt M D 139 p g Ilu t t d Ch l C Th m P b-  
li h Sp gf ld Ill 1958 P \$4 50

This is an erud te st mul t g app oach to psychiatric treatment The book is thought prov k g and d m nstrates c n d able re- se ch and thinking much of it original It attempt to expl in empiric l tr atment method by carefully work d out sc ntific evi d nce s me of which h s adm ttedly not b n subj cted to experimental or clinical valid t on The auth r points out th t the h st y and cl n al ex mnat on sho ld b augmented by things th t c n b tested objecti ely In this con ct o he give an explan ti n of the dr nalin mecholyl test and d cribes hi use of the t st as an n d c to of pr gnosis and pot ntial re pons ve s to treatment An excellent summ ry of the var ou types f electrotherapy and of the various new r types of ch motherapy is n luded In a ch pter on front l lobotomy the a thor advocates th form of treatm nt in some ca s The ch pter on p ychotherapy nvolves primarily a discuss on of how working through c mp res to Pavl v s laws of the high r nervous activity of the cerebr l cortex This book has m it becaus r ther than rely ng on empir c sm it attempts t app oach the various psychi tric tre tments objectiv ly and g ve to them a scientific ex planation It of interest p marily to psy hiatrists and would ppeal more to the organic or eclect c m n in the fi ld and pr bably less to the strictly dynamically oriented yet t s well worth reading as an e cellent summary (with n extensive bibli graphy) of ne of th tre mpts to correlate th observed om tophysiol g factors in psychiatric tre tment with the psychic factor

—DASIL C SMITH *Lt Col USAF (MC)*

BIOLOGY OF NEUROGLIA C mp l d d d t d by W ll m F W dl Ph D  
Sc D 340 p g ill t t d Charl C Th m P bl h Sp gf ld  
Ill 1958 P \$8 50

The term n u oglia refers to veral h ghly specialized but p m ne t cell types f und n the nervous system The first funct on signed these c lls and indeed the one still de cribed in neuroan tomical

texts is that of serving as the connective tissue of the nervous system—the nerve glue in translation. As time has passed it has become clear that the microglia, one of the neuroglial types, acts as a scavenger of the nervous system and is in fact derived from dermal wandering cells originating from vascular elements. The function of the remaining cell types, the astrocyte and the oligodendrocyte, however, has remained unknown. The conception of the latter function as a connective tissue has become less popular. It has now been suggested that the astrocyte plays a role in controlling the neuronal environment by acting as an intermediary between the blood stream and the neural parenchyma. The oligodendrocyte is thought possibly to play a role in the formation and maintenance of the myelin sheath and perhaps also to be involved in nerve transport.

The present book emanates from a meeting of researchers in March 1936 when some of these problems in the morphology and physiology of the neuroglia were discussed. The book is directed to the researcher and the specialist, should especially be recommended to those who are concerned with the physiology of the nerve cell and of the perineuronal environment. Of central interest were the electron microscopic descriptions of the glial elements and particularly of the mysterious neuropil or interstitial space of the gray matter which now for the first time receives elucidation. Of great interest also were the sections relating to the problem of myelin formation and maintenance and the possible relation of the oligodendrocyte to this process.

*Biology of Neuroglia* represents an excellent treatment of the present understanding of the morphology and function of these much neglected elements of the nervous system.

—ROYALD E. MYERS, Capt. MC USA

**ANOMALIES OF INTESTINAL ROTATION AND FIXATION (Including Mesentericoparatal Hernias)** by Roberto L. Estrada B. Sc. M. D. C. M. D. Surg. (McGill) F. R. C. S. (C) F. A. C. S. 161 pages. Illustrated. Charles C. Thomas, Publisher, Springfield, Ill. 1938. Price \$6.50.

This monograph represents one of the few reviews on this subject to be printed, as most of the literature consists of isolated case reports. The author reviewed the literature from 1786 through 1936 with the idea of obtaining a clearer understanding of the way abnormalities of intestinal rotation and fixation are produced. An anatomic and embryologic background is developed which will be very valuable to the surgeon, radiologist and anatomist.

With the idea of standardizing the nomenclature as an aid for future publications and analysis, the author develops his own classification. He designates the following stages in the development of intestinal anomalies: the stage of deviation, the stage of fixation, the stage of rotation, the stage of deviation and fixation, the stage of deviation and rotation, the stage of deviation and fixation and rotation, the stage of deviation and fixation and rotation and fixation.

into the abdomen and the tge of f xat on Prope ly he stresses the midgut as the ffend ng organ in all cases

Based on this review and n 29 of the author s own cases h further elucidates the symptomatology diagnostic aspects and treat ment when th surgeon is confronted with an an maly in the operat ng rom From a clinical viewpo nt probably the most important sections are on append c tis in non r rat on and on mesentericoparietal he ni tions

Complete with excellent diagr ms x ray p ctures and b bliography th s volume should do much to clarify in the clinician s mi d a gener ally m sunderstood problem

—LESTER J POPE Capt MC USN

CLINICAL PROCEDURES IN OCCLUSAL REHABILITATION by S Ch l B k D D S F A C D 326 p g 936 ll tr t on 428 f gur W B S und C Ph lad lph Pa. 1958 P \$16

The author of th s volume presents the subject of occlu l reh bili tat on in a reveal g mann To many dent t occl al eh bilitat on ha been avoided as a pr bl m area or a ph e of p ct e t o diff cult to t t mpt without particip tion in postgraduate traini g and th purchase of complic ted equ pm nt The lim tat o s controlling suc c ssful rehab litation are t e ed The thorough kn wl dg of what not to tre t seems as paramount to succ ss as the ab lity to treat correctly tho e c ses selected Th r quired select on of a specific pr ci on art cul tor is dispens d with s merely a compl cat on to pr gress Blind adherence to the use of th hinge axis for pat e t who fo y rs have been function g in eccentric posit o s may invite trouble Geom tric fo mul s complicated th res on occlu n and function of the temp romand bular joi t a e n t essent l to the suc ce sful restorat on of occlu About half of the book d ls clearly with step-by step procedur for the prep r t on of teeth nd the l b r tory pr dures nec ssary for complet on of th c se Full coverage re torations fixed d removabl part al dentures and internal attachments are pr cisely described Emph s s is placed on pictures for e ch clinical tep The b l ce of the bo k is devoted to a pract cal grouping of p t ents needing occlusal recon truction with step-by step procedur s for each group L mitation f materi ls are discussed s are a t m c abnormalities and muscul habits The book is ea y to read and th techn cs ea ily followed It s high ly r commended a a v luable addition to the person l l b arie of all d t sts —THEODORE E. FISCHER C I USAF (DC)

VIRAL ENCEPHALITIS A Symp m F fth Annual S f M t g f h H t N l g al S ty T M d l C t H ton T C mpled and d ted by W l l m S F ld and Rus ll J Bl tt 225 p g ll t t d Charl C Th m Sp ngf ld Ill 1958 P \$7

During the p t five years the Houston Neurological Society h sponsored annual symposia e ch b sed on a ngle bro d topic The

contributors highly qualified in their specific fields of these topics from their own points of view. A serious and successful attempt is made to integrate present-day knowledge and concepts regarding these important topics.

This 225 page neatly bound and clearly printed book contains material presented at the March 1, 1957 meeting devoted to viral encephalitis. The papers contain much interesting data not available in standard textbooks. A reasonable classification is offered and its defects carefully noted. Exceptionally good is a paper on the epidemiology of western equine and St. Louis encephalitis which points up the importance of arthropod transmission and wild animal reservoirs in the viral diseases. A superb paper on clinical and laboratory diagnosis contains clear tables delineating and contrasting the important viral affections of the nervous system. A detailed but easily read discussion of postencephalitic sequelae indicates the prognostic significance of a patient's age and the concepts of a progressive or chronic viral encephalitis are to be questioned. A long almost monographic and beautifully illustrated paper describes the pathology of viral diseases in man characterized by nuclear inclusions. Including this topic in an otherwise well balanced symposium without providing a brief account of pathologic changes found in more common varieties of viral central nervous system disease is unusual. Control of neurotropic viral diseases is successful in rabies and poliomyelitis and recent trends in therapy are dealt with methodically and well in the final paper.

As in most symposia the discussions following each paper are entertaining and valuable. The principal defect of this and similar works is the lack of an index. The book is fairly inexpensive and in a few hours gives a thoughtful reader a good picture of viral encephalitis as we see it today. It is the best single volume on the subject and is recommended highly to neurologists, internists, pediatricians and general practitioners.

—HENRY W. HOGAN, M.D., M.C., USA

**OCULAR ALLERGY** by Fredrick H. Theodore, M.D. and Abraham S. Blois, M.D. with chapters by William B. Sherman, M.D. and Robert S. Coles, M.D. 420 pages illustrated. The Williams & Wilkins Company, Baltimore, Md. 1958. Price \$12.

This is the first recent book on ocular allergy and the need for one has been evident for many years. Ocular allergy forms an increasing part of ophthalmologic practice. Many allergies are not recognized as such while others are erroneously so diagnosed.

The authors have thoroughly covered those conditions known to be allergic in origin and have called attention to many conditions that could be possibly explained by hypersensitivity. The text is a practical one and those interested in allergy will enjoy reading it. The book is well written, it has a good index and bibliography and few typographical errors. —NELSON O. OLSON, Capt. MC, USN

A GUIDE TO HUMAN PARASITOLOGY FOR MEDICAL PRACTITIONERS  
 (Blklkd S uthw ll) id by T H D y O B E M D  
 D T M 6 h d t n 222 p g w th thr c l d pl t d 119 ill str  
 t t th t t. The W ll m d W lk C B l mor Md 1958  
 P \$7 00

This book a guide for cl n cians who do not have the assistance of a clinical laboratory and must depend up n their own examinatio of samples for laboratory diagnosis It is assumed that the re der has h d no experience in the field and the text is des gned to develop proficiency in the diagnosis of p rasitic infect ons

An introd ct on to the use of the m cro cope and the preparation and ex minat on of s mpl s is followed by a discuss on of the variou clas es of para tes The habitat morpholog cal char cters life history pathogenicity diagnos s and prevention are pres nted in con c manner for each par sit There are numerous keys which aid in id ntification and the life hi to ies a diagr mm tically presented in a simplified manner Further identif cat on of para ite s aided by th 119 ill str tions Although this text was written for the cl nician it may be used by anyone inte ested in attaining proficien y in ident f cation of human p ras tes —JOHNE STAUCH Capt. USAF (MSC)

MODERN TRENDS IN ENDOCRINOLOGY Ed t d by H G d ~H H M D  
 F R C. P 311 p g llus t d P l B H be l m d l b k  
 d p itm t f H rp & B th N w York N Y 1958 P \$13 50

This volum which const t of 21 chapters lives up to its title admirably It covers most of the m jor advan es in endocrinol gy today and indicates the l kely lin of future progr s Th art cles are for the most part informative nd concise with an excellent up-to-date b bliogr phy Th majority of the author are well establ sh d Br t sh nvestig tors including Pitt R vers Randall McCance Black Prunty and Cope Th reviewer and Pr fessor Swan of th Mayo Clinic we e the nly Amer can authors in the volume

A mght be expected the subject m tter is quite va id ra ging from the theo etical asp cts of the significance of the str ss concept in cl nical medicine and h rmon l f ctors in breast dev l pment and milk secr tion to the very practical problems of uses of tero ds in th treatment of rheumatic ad allerg c disorde s and endocrine therapy of malignancy of the bre st and prostat P rticuly outstanding in this volume the article by Dr Randall ntitled Endoc ine Facto s in the Syndrome of Diabet s M llitus which rep esents the most con c se summat n of the extens e investigati ns done by this inve t gator nd Prof or Frank You g that has y t appeared in p int

The art cle by Gilliland on the etiology and tr atment of exophthalmos while quite dequ te could possibly have been improved by refer nce to recent adva ces in hypophysectomy and stalk transe tion in the t eatment of th s conditi n Similarly the article concerned with tests of thyroid functi n d d not have a discussion of a butanol extract bl

iodine and might have been of more benefit to many physicians had it included a brief discussion of the current controversy concerning hypometabolism without hypothyroidism. Neither of these chapters referred specifically to the use of thyroid stimulating hormone or prolonged treatment with thyroid extract in the diagnosis of hyperthyroidism especially when associated with the problem of exophthalmos without other evidence of increased thyroid activity.

It is a primary datum of observation that one does not criticize a work for not doing what it never intended to do. Obviously the whole field of endocrinology could not be covered in such a volume and one hopes that the reception of this work will be sufficient to stimulate further issues in this much needed series. There is no question however that the subject matter presented in this volume is as broad a coverage of the field as could be done in the space allotted.

This book should be in every medical library and will undoubtedly be of considerable value to endocrinologists as well as those internists and gynecologists with an interest in this subject. The print is legible and large and the changing styles and balance of the subject matter is quite refreshing and makes for enjoyable reading. I believe that the distinguishing quality of this volume however is that it is more up-to-date than many current periodicals. In addition it provides a very refreshing insight into authoritative British thinking on a variety of important subjects.—PAUL J. ROSCH *Capt MC USA*

**BONE AND RADIOSTRONTIUM** by Arne Engstrom, Rolf Björnerstedt, Carl Johan C. M. d. on and Arne Nel on. 139 pages illustrated. John Wiley and Son, Inc. New York, N. Y. 1958. Price \$8.75.

This short monograph consists of a review of experimental work performed by the authors on the metabolism of radiostrontium, the physiology and micromorphology of skeletal tissue and the development of a dosimetric model based on these studies for an estimation of the maximum permissible dose of Strontium<sup>90</sup>.

The introductory chapter is concerned with metabolism of strontium in the mammalian organism, well documented with 70 references, many of them appearing in the American literature. The language is not always fluent and a few typographical or translator's errors occur.

Three chapters discuss the distribution and ultrastructure of bone salts and the distribution of Sr<sup>90</sup> in the skeleton. The techniques used in this study, x-ray microscopy or historadiography, micro-interferometry and autoradiography, are adequately discussed and described. The illustration quality is good though the lack of labelled anatomic landmarks may make orientation difficult.

Theoretical calculation of the dose rate distribution from Beta emitters comprises a whole chapter. One wonders whether such a sophisticated development of dosimetry (30 pages) is warranted as the authors have chosen as their model for spongy bone an infinite sandwich



of alternate layers of radioactive and non radioactive material this model according to their admission is only approximate

An attempt at estimation of the maximum permissible body burden of Strontium<sup>90</sup> is made in the last chapter and is actually based on a system of dosimetry commonly used rather than on the system developed by the authors. As a first approximation the dose to bone is calculated to be 5.8 mrem per day per gram of bone which estimate assuming Sr<sup>90</sup> is concentrated homogeneously in the osseous portion of bone is reduced to 25 mrem per day. Taking into account the deposition of Sr in hot spots where the maximal dose rate may be 10 times higher estimates of local dose rates in bone of from 300 to 500 mrem per day per gram of bone are made by the authors. This is from a total body burden of 1 uc of Sr<sup>90</sup> the current maximum permissible body burden. On the basis of the studies the authors conclude that a body burden of less than 0.1 uc Sr<sup>90</sup> is tolerable.

The experimental data well presented and the techniques described will doubtless be of value to other investigators. Final development of an estimate for the maximum permissible body burden of Sr<sup>90</sup> is not as rigorous as the material which preceded it and will probably be subject to critical review.—THOMAS G MITCHELL, Lt. MSC USN

CARDIOVASCULAR COLLAPSE IN THE OPERATING ROOM by H. B. R. E. N. I. f. I. D. d. M. S. S. d. M. D. F. w. d. by W. R. H. C. I. M. D. 197 p. g. ll. t. d. J. B. L. pp. 11 C. Ph. l. d. lph. P. 1958. Pn. \$6.

This volume encompasses the inclusive field of cardiovascular collapse and differentiated from the more dramatic and less precise term cardiac arrest in an effort to correlate the numerous causes and effects of the physiological imbalance resulting in operating room emergencies. It recognizes that there is now no uniform method for classifying data since the criteria for classification and interpretation vary so greatly. Emphasis is placed on the multiple predisposing and precipitating factors involved. Utmost stress is made on adequate preoperative evaluation of the patient's condition and the correction of basic pathophysiological mechanisms. Only full cooperation of the entire medical staff can fully assess the patient as a surgical risk and institute corrective measures for existing deficiencies. The prophylactic measures begun with the first physical examination of the patient must be carried through by an alert and cooperative surgical team where effective communication exists.

The book is well organized and logically presented. The inadequacies of the present reporting methods are noted and 775 cases are analyzed to fully implicate the multiple factors involved. Causative mechanisms are discussed individually and completely. These include the management of preexisting cardiovascular and pulmonary disease, hypovolemia and anemia, various endocrine abnormalities and the peculiar problems encountered with the extremes of obesity, drunkenness, racial variations and specific diseases. The blood coagulation distur-

ances and transfusion reactions are reviewed and diagnostic and therapeutic measures are suggested. Thirty three cases are presented by protocol and primary causes of the complications are indicated. Prevention of catastrophe depends on an awareness of special problems and the institution of the necessary precautions. The anesthesiologist's perception of early signs of impending danger are of greatest importance. Constant watchfulness is the keynote in successful diagnosis and treatment and this cannot be replaced by monitoring devices. Treatment is divided into specific and nonspecific elements and a complete emergency treatment cart is described.

The tables are easily read and the figures are accomplished with clarity. The bibliography is extensive and the index is complete. This book is recommended not only for anesthesiologists but for all physicians who wish to guide a patient successfully through a surgical procedure — ROBERT E. LAU Col USAF (MC)

*CLINICAL ORTHOPAEDICS* by Anthony F. DePalma editor-in-chief with the assistance of the Associate Editors. The Board of Advisory Editors: The Board of Corresponding Editors. No. 10. Fall 1957. 367 pages illustrated. J. B. Lippincott Company, Philadelphia, Pa. 1957. Price \$7.50.

Volume 10 of *Clinical Orthopaedics* is dedicated to Phemister of Chicago, a great general surgeon who based on his experience in Germany has probably contributed more to clinical application of bone pathology and bone physiology than any single man in our century. The volume contains four sections dealing with the affections of growth centers, the part of basic physiology of metabolic bone disorders which could not be included in Volume 9, general orthopedics and the fourth section entitled Items — a total of 30 articles. The editor has again shown his ability in presenting broad aspects of orthopedics and borderline fields.

As to the practical value contained in the individual papers, McElvenny's discussion of the treatment of hip fractures is probably the most outstanding. The general attitude toward that problem is one of resignation to the necessity of accepting a high percentage of undesirable results. McElvenny's discussion based upon clear indications, meticulous technic and 20 years of experience shows ways of avoiding disappointments which have been entirely successful in his hands. Of great value to the orthopedist also is Garland's article on long-range effects of radiation on bone, written with great clarity and authority. Martin and Pipkin's article on treatment of avulsion of the ischial tuberosity has beautiful sketches illustrating the mechanism of injury. The original mode of presentation certainly enhances the teaching value of the paper. Calvo presents a nice piece of research on the growth of the female adolescent spine which indicates that the criteria generally used at present are not entirely reliable. Katz presents an end result study of 111 cases of Legg Perthes disease treated by various forms of non weightbearing on the affected side. His conclusions

are extremely cautious and should be because the results show fall short of the ones seen in entirely untreated cases

One wonders whether the importance of the acetabular index is not overemphasized as it does not seem to have any bearing on the function or on the development of late complications. It is interesting to note the great variations in the present attitude toward credit given to previous writers on the subject. Thus Howarth devoted almost three pages to the history of the slipping of the upper femoral epiphysis while J. E. M. Thomson reviewed turnbuckle correction in fresh fractures apparently unaware of the original work of Fabricius Hildanus in 1629 and the extensive use of the method of Hackebusch in Germany during World War II. The volume is of great interest and value to the orthopedist and beyond that to anyone interested in conditions affecting the skeletal system.—ERNST DEHNE *C I MC USA*

PHARMACOLOGY IN MEDICINE A Clibert Tibbels edited by V. I. A. D. H. Ph. D. M. D. 2d ed. 1273 pages. Illustrated. P. Bl. h. d. by M. G. W. H. H. B. k. C. I. B. k. t. D. New York, N. Y. 1958. Pp. \$19.50.

This comprehensive volume of multiple authorship is intended as a textbook and reference a purpose generally well fulfilled. The material is well arranged and major headings divide the chapters into drug usages, organ systems, and specific therapeutic agents. The chief advantage of its multiple authorship is the presentation of authoritative information and opinions on a myriad of subjects. Individual drugs are discussed from the standpoint of mechanism of action, effect in the body, therapeutic action, and available form. The discussions of physiology and pharmacology are written simply and understandably with considerable emphasis placed on drug action and least emphasis on the clinical aspects.

This book is well written, fulfills a definite need as a pharmacology text, and is a useful reference for students and practitioners. Its chief deficiency is from the clinician's standpoint—and this is not too serious—is its brevity regarding actual drug dosage and clinical application.—R. J. PEARSON *J. C. PL. MC. USN*

CARBON DIOXIDE THERAPY A. N. W. phylog. I. g. I. T. m. f. N. D. d. d. t. d. by L. J. M. d. M. D. 2d ed. 541 pages. Illustrated. Charles C. Thomas. P. Bl. h. Sp. g. f. l. d. Ill. 1958. Pp. \$14.50.

This volume sponsored by the Carbon Dioxide Research Association merits attention as a handbook on the use and present status of carbon dioxide in the treatment of nervous disorders. The several tested techniques of carbon dioxide therapy, their indications and contraindications of their use, and the nature and extent of the clinical results achieved are discussed in great detail. The collected papers provide a summary of the available information and emerging understanding relative to the physiologic basis of this form of treatment. In addition to its importance to the psychiatrist, the symposium



THE IMPACT OF THE ANTIBIOTICS ON MEDICINE AND SOCIETY M o-  
 g ph II I t t t / S l d H t l M d T b N w Y k  
 A demy / M d Ed d by I g G l d t M D 222 P 8  
 I t t l U t P I N w Y k N Y 1958 P \$5

This book is composed of several chapters each dealing with some phase of antibiotics and is a compilation of papers given at the Institute of Social and Historical Medicine of the New York Academy of Medicine. The historical development of these drugs has been covered in such chapters as The Microbiology of the Soil and the Antibiotics and The Role of Industry in the Mass Production of Antibiotics. It covers in general fashion the effects of these drugs in our present society as they influence infectious diseases. The book is of interest for those who desire a general historical review of the development of the antibiotic and the present status in our society.

DOSS O LYNN C I MC USA

DIAGNOSTIC MEDICAL PARASITOLOGY by Edu d A M k II Ph D  
 M D d M II V g M A Ph D 276 p g 115 f gur  
 I d g 5 l W B S d C mp y Ph l d lph P 1958  
 P \$7

Markell and Vogt wrote this book to present in readily available form the essential facts needed by the medical student and clinical laboratory technician for the diagnosis of human parasitic disease. In this venture they have succeeded admirably.

The book is well organized and written in a clear and simple manner. The 115 figures and notes 276 pages contribute significantly to the usefulness of the text. They have obviously been carefully chosen for their practical diagnostic utility rather than for mere encyclopedic coverage of the subject. The introductory chapters state the purpose and frame of reference of the book and provide a lucid discussion of the concept of parasitism. Succeding chapters group the various parasites according to their organ system of predilection rather than following the classical phylogenetic format. This parallel approach of the physician examining patient—the effectiveness of the symptomatic and organ systems involved identification of the etiologic agent comes later. The short chapter on pseudoparasites and pitfalls will alert the unwary and alert the for whom parasitologic diagnosis is not a primary occupation. Special methods procedures and material are included in form well adapted for ready reference. The treatment of parasitic disease has been purposely omitted since therapy is changing too rapidly for book to main current.

Although *Diagnostic Medical Parasitology* was written primarily as a textbook military physicians and laboratory personnel will find it valuable as a practical ready reference manual to be used in conjunction with the more extensive texts on clinical parasitology and tropical medicine.—HERSCHEL E GRIFFIN Lt C I MC USA

AN INTRODUCTION TO EXPERIMENTAL SURGICAL STUDIES by W. J. Dempsey F. R. C. S. 463 pages illustrated Charles C. Thomas Publisher Springfield, Ill. 1958. Price \$10

This book is intended primarily for the postgraduate surgical student engaging in experimental surgery. Any surgeon interested in understanding the relationship between clinical and experimental surgery would greatly benefit by it. The great advances in modern surgery are the direct result of applied physiologic principles and experimentation. The text is easy to read, entertaining and matter-of-fact, so typical of the British author. It is well indexed and illustrated. The bibliography is copious, comprehensive and is conveniently located at the end of each topic discussed. The book is divided into an introduction and eight chapters, and throughout the relationship of clinical and experimental surgery is well correlated, providing a wide range of references and critical commentary which serve as a springboard to one interested in experimental surgery. The editor is to be congratulated on the concise and lucid manner in which he reveals the close relationship between clinical and experimental surgery.

—OAFLEY K. PARK, Lt Col USAF (AC)

INTESTINAL OBSTRUCTION by Claude E. Welch M.D., D.Sc. (Hon.) Illustrated by Muell McLatchie M.D. 376 pages illustrated The Year Book Publishers Inc. Chicago Ill. 1958. Price \$10.50

The organization of this volume into general considerations (anatomy, diagnosis and etiology), fundamental aspects of therapy (time of operation, intubation and replacement therapy) and types of obstruction is fully appreciated when used for ready reference. Presentation style and descriptive terms used result in easy and interesting reading without the usual excess of tables and graphs. The precise manner is uncluttered with multiple variations or repetitive t

Chapters on tubing and postoperative obstruction as informative as any this reviewer has read. Treatment presented in a logical and physiologic manner as each type of obstruction is discussed.

Applying the essentials of this text to clinical surgery will lead to improved results in diagnosis and treatment of intestinal obstruction. While not a medical student's book it is highly recommended for residents and practicing surgeons.

—VICTOR C. STRATTON, Capt. MC, USN

DYNAMICS OF PSYCHOTHERAPY. The Psychology of Psychiatry. By P. I. M. Symonds. Philadelphia: W. B. Saunders Company, 1958. Pp. 634. \$6.50.

This third volume of *Dynamics of Psychotherapy* is concerned with the role of the therapist, his responsibilities, goals, and techniques. Symonds regards interpretation as the chief function of the therapist in psychotherapy, and this interesting and controversial issue is the topic of 10 of the 19 chapters. When to intervene, when to clarify, when to question, when to keep silent—all are considered. What patient resistance means and how it should be handled, how transference is managed, and how the patient's anxiety is related to the therapist's interpretation are also detailed. The therapist's use of reassurance (and all therapists use it), suggestion, commands, and advice is explained.

This volume should be of use to the ordinary practitioner who is interested in psychotherapeutic aspects of medicine, and to the beginning psychiatrist who would like a systematic textbook which will tell him not only what to do, but why to do it.

—WALTER L. WILKINS, Command. MSC, USNR

RECONSTRUCTIVE AND REPARATIVE SURGERY. By H. M. Y. M. D. F. A. C. S. 2d ed. 1115 pages. With 1030 illustrations. 1958. \$11.50.

This is an excellent, well-organized textbook on plastic surgery. It is divided into five sections, and each section contains excellent bibliography with ample illustrations.

The first section deals with general principles of plastic surgery, with a particularly good portion devoted to a discussion of grafts. The next three sections are appropriately divided and refer to the respective regions of the body. The fifth section contains a group of illustrated cases which makes interesting reading. The present edition is the first revision in 10 years, and most of the changes concern the treatment of burns, use of antibiotics, and modern concepts of transplantation.

The book has much useful material and is presented in a clear, concise manner. General surgeons should find it a helpful and valuable text to have on hand, especially when the services of a qualified plastic surgeon are not readily available.

—FERDINAND V. BERLEY, Capt. MC, USN

## New Books Received

Books received by the U S Armed Forces Medical Journal are acknowledged in this department Those of greatest interest will be selected for review in a later issue

- PRINCIPLES OF INTERNAL MEDICINE** Editors *T R Harrison Raymond D Adams Ian L Bennett Jr William H Resnik George W Thorn and M W Wintrobe* 3d edition 1 839 pages illustrated The Blakiston Division McGraw-Hill Book Company Inc New York N Y 1958 Price \$18 50
- THE ACUTE ABDOMEN** by *William Requarth M D* Foreword by *Warren H Cole M D* 2d edition 313 pages illustrated The Year Book Publishers Inc Chicago Ill 1958 Price \$6 50
- A TEXT ON SYSTEMIC PATHOLOGY** Volume I edited by *Otto Saphir M D* 865 pages with over 800 illustrations Grune and Stratton Inc New York N Y 1958 Price \$32
- A PHYSICIAN LOOKS AT PSYCHIATRY** by *Jacques M May M D* 189 pages The John Day Company New York N Y 1958 Price \$3 50
- PATHOLOGY FOR THE PHYSICIAN** by *William Boyd M D* Dipl Psychiat M R C P (Edin) Hon F R C P (Edin) F R C P (Lond) F R C S (Can) F R S (Can) LL D (Sask) (Queen's) D Sc (Man) M D (Oslo) 6th edition thoroughly revised 900 pages 489 illustrations and 12 plates in color Lea & Febige Philadelphia Pa 1958 Price \$17 50
- THE DOCTOR IN PERSONAL INJURY CASES** by *Haold A Leben* on Foreword by *Sidney S Greenspan M D* 123 page Published by The Year Book Publishers Inc Chicago Ill 1958 Price \$4
- THE PSYCHOLOGY OF MEDICAL PRACTICE** by *Ma c H Hollend M D* 276 pages W B Saunders Company Philadelphia Pa 1958 Price \$6 50
- MILESTONES IN MODERN SURGERY** by *Alfred Huutz M D* and *George A Dagensheim M D* with foreword by *J Englbert Murphy M D* 520 pages illustrated Paul B Hoeber Inc Medical Book Department of Harper & Bros New York N Y 1958 Price \$15
- A MANUAL ON CARDIAC RESUSCITATION** by *Robert M Hosler M D* F A C S 2d edition 208 pages illustrated Charles C Thomas Publisher Springfield Ill 1958 Price \$5 50
- VARIABLES RELATED TO HUMAN BREAST CANCER** by *V Elving And so Haold O Goodman and Sheldon C Reed* A Study from the Night Institute of Human Genetics 172 page illustrated The University of Minnesota Press Minneapolis Minn 1958 Price \$4
- CLINICAL STUDIES IN CULTURE CONFLICT** edited by *George S ua d* Ph D 598 page illustrated The Random House Company New York N Y 1958 Price \$7



THE EFFECTS OF A THREATENING RUMOR ON A DISASTER STRICKEN COMMUNITY by Ell tt R D zig P l W Th y and L l R G lant D Study N 10 D R ar h G p D i f Anthr p l gy and P y h l gy P pa d i r F d l C l D f Adm n tr t and Th D R ar h G p (F m ly Th C mm tt D Stud ) 116 p g ll tr t d P bl o 517 N t al A d my f S en N t on l R s arch C un l Washngt D C 1958 P \$2

A PRIMER OF CEREBRAL PALSY by J ph D R M B M D F A A P F A A C P and Hym R S b l // B A M B M D F A A O S F A A C P P bl t on N 329 Am L tur Se A M gr ph Am L tur P d t cs ed t d by J km A A d M D 77 p g ll t t d Charl C Th m P bl h Sp gf ld Ill 1958 P \$4

EGO STRUCTURE IN PARANOID SCHIZOPHRENIA A N w M th d f E l g P o j t M l by L J Zuck Ph D P bl cat on N 331 Am an L tur S A M g ph Th Ban t D on f Am an L tur in P y h l gy d t d by M lly H r w Ph D 186 pag ll t d Charl C Th m P bl h Sp g f ld Ill 1958 P \$5 50

CIBA FOUNDATION SYMPOSIUM ON THE CEREBROSPINAL FLUID P d t C ul t and Ab pt Ed t f h C b F und G E W W l tenb lm O B E M A M B B Ch and C l M O C nm B Sc 335 p g w h 141 ll t t L ttl B w & C mpany B M 1958 P \$9

COMPLETE DENTURE PROSTHESIS by D l H G bl D D S and O M Dr D D S F m ly by Rud lph O S bl D D S F A C D 4 h d t on 542 p g w h 310 f gur W B S und C mpany Ph l d lph P 1958 P \$11

FRACTURES AND OTHER INJURIES by h M mb f th F t Cl f th M h tt G l H p t l d f th F lty f th H rv d M d l S h l d d by Eduw F C M D D w g by M l M L t h M ll Ph t gr phy by D ld W th Ed t l B d J ph S B rr M D B d f d C M D Cl d E W l h M D J m C W h t M D Eduw F C M D 863 p g ll d Th Y ar B k P bl h l c Ch g Ill 1958 P \$28

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DIAGNOSTIC LABORATORY HEMATOLOGY by G g E C tu ght M D 2d d t d and larg d 250 p g ll st d Grun & St tt I N w Y k N Y 1958 P \$6 50

ADVANCES IN ELECTROCARDIOGRAPHY d d by Ch l E K m nn B S M D M d Sc D F A C P 280 p g ll t d G & St tt I N w Y k N Y 1958 P \$6 75

HEALTH YEARBOOK 1957 mpl d by Ol E By d Ed D M D F A P H A 278 p g ll d S an f d U ty P S an f d C l f 1958 P \$5 50

ALCOHOLISM by Am ld Z P f // M D F w d by S C F M D F A C P 98 p g ll d G & Str l N w Y k N Y 1958 P \$6 50

# INSTRUCTIONS FOR AUTHORS

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Fleming A, Young M, L. Suchet J and Rowe A. J. E. Penicillin content of blood serum after various doses of penicillin by various routes. *Lancet* 2: 621-624 Nov. 11 1944

Cabot R. C. Pernicious and secondary anemia, chlorosis and leukemia. In Oler W. (editor) *Modern Medicine* 3d edition. Lea & Febiger Philadelphia Pa. 1924 Vol 5 pp 33-100

## FIGURES AND TABLES

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## INSTRUCTIONS FOR AUTHORS

(See page 100 for details)

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UNITED STATES  
GOVERNMENT PRINTING OFFICE  
WASHINGTON 1958

# Monthly Message

The United States edition of the NATO Emergency War Surgery Handbook has just been published by the Department of Defense. Its title is EMERGENCY WAR SURGERY NATO HANDBOOK. The NATO Handbook itself was published by SHAPE and was the result of studies and compilation by a committee of NATO under the direction of the then Brigadier General Wilford F. Hall, USAF (MC). The committee consisted of representatives from Great Britain, France, Canada, and the United States, with consultation and advice from representatives of other NATO nations.

This book, originally published in English, has already appeared in a Turkish edition, and doubtless other countries will republish it. The United States edition, a slightly smaller and condensed version, can be readily carried in one's pocket and is an excellent digest of emergency war surgery, as its name implies. A similar small edition will in all probability be published by Canada and Great Britain. All medical and dental and veterinary officers in the armed services will receive a copy of this book, and it also may be obtained from the Government Printing Office at a cost of \$2.25. Its chapters include information on factors in production of war injuries, factors complicating war injuries, sorting initial care and evacuation, anesthesia and analgesia, regional injuries, and a glossary of drugs.

Brigadier General Sam F. Seeley, MC, USA, the Chairman of the NATO committee, was assisted by Colonel Joseph R. Shroff, MC, USA, Captain Robert B. Brown, MC, USN, and Colonel David Gold, USAF (MC), in the preparation of the United States Armed Forces edition.

I recommend this book to every member of the medical, dental, pharmaceutical, and osteopathic professions and to all students in their schools.

*Frank B. Berry*

FRANK B. BERRY, M.D.  
Assistant Secretary of Defense  
(Military and Medical)

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## Foreword

Th U t d St t Arm d F M d l J l th m d m f d  
m g f m t f dm t t d p f l t t ll  
m d l p l f h D p tm f D f Th A S y  
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ff Nur C rp ff d ff f th V ry C rp f h  
Arm d F d h m d l lt f th A my N vy d Aur F  
t b m m p f p bl t in h J m l

FRANK B BERRY M D

A t t S t ry f D f (H lth d M d l)

MAJOR GENERAL SILAS B HAYS

S g G l U t d St t A my

REAR ADMIRAL BARTHOLOMEW W HOGAN

S g G l U t d St t N y

MAJOR GENERAL DAN C OGLE

S g G l U t d St t A F

# UNITED STATES ARMED FORCES MEDICAL JOURNAL

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Volume IX

September 1958

Number 9

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## CLINICAL TRIAL OF PASTEURIZED POOLED HUMAN PLASMA

WILLIAM C. LEVIN, M.D.  
TRUMAN G. BLOCKER, Jr., M.D.  
E. FRANK DUNTON, M.D.  
MELVIN A. CASBERG, M.D.

IT is generally accepted that with the exception of whole blood, the best blood volume expander is pooled human plasma itself. This material offers a number of technical advantages over whole blood. No typing or cross matching technics are required prior to its administration, it can be stored for years, and technical problems introduced by the collection, storage, and administration of the various blood cells are avoided. Synthetic plasma expanders are inferior to pooled plasma for a number of reasons. Anaphylactoid and pyrogenic reactions, hemorrhagic manifestations, sludging of blood, and other untoward clinical reactions have occurred following the use of these synthetic compounds. There is also the theoretical objection that retention of such compounds in the tissues may either exert a carcinogenic effect or produce dysfunction of the organs serving as storage sites. This has been suggested by follow up studies of patients in Germany who received polyvinylpyrrolidone during World War II.<sup>1-3</sup>

However, experience with lyophilized pooled plasma has produced plentiful evidence that it serves as an effective medium for the transportation and dissemination of the serum hepatitis virus. With very large pools, this has been a most distressing problem, producing a fantastically high incidence

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Ft. M. th. D. partm. nt of I. t. r. l. Med. n. D. partm. t. f. Surg. ry. (Pl. stic Surg. ry.  
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Br. ch. G. I. t. T.

of serum hepatitis reported as high as 70 per cent. This problem has prompted the development of two main lines of investigation: (1) the fractionation of plasma proteins since the virus is presumably concentrated in one of the fractions which can be discarded thus permitting the concentration of virus free albumin which exerts a powerful oncotic effect and (2) the search for an effective means of inactivating the virus without significant altering of the biologic properties of the plasma constituents.

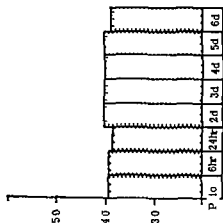
The fractionation program has been most successful from a scientific and technological standpoint but neither ordinary civilian medical needs nor the broader military requirements are completely satisfied by the products of plasma fractionation. In the first place this is an expensive program from the standpoint of financial cost as well as a large cost in man hours and the low yield of this process. The administration of albumin produces chiefly an oncotic effect while probably making only a limited nutritional contribution. Pooled plasma may exert a somewhat broader effect (such as transfer of immune bodies and coagulation factors). Finally fractionation by adding a number of tedious and time consuming steps to the processing of plasma does not lend itself to convenient logistic planning for stock piling and thereby for ready and adequate availability for major civilian catastrophes and military requirements.

Efforts to develop an effective means of plasma sterilization have produced a number of techniques. The only two which have apparently been successful in this direction are the storage of liquid plasma at elevated temperature for six months and the pasteurization of pooled plasma. The former method though presumably effective in making the virus nonviable and in failing to produce overt evidences of alteration of biological activity of the plasma is not wholly satisfactory in the planning of any major stockpiling effort and would be completely impracticable in the event of a nationwide catastrophe inasmuch as the time required for processing is excessive. Therefore the development of pasteurization presented the attractive possibility of solving the knotty logistic problem of rapidly producing large quantities of pooled human plasma which would at once be safe to administer and biologically effective as a blood volume expander.

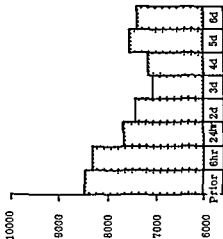
The present study was planned to evaluate both of these points: safety of administration and oncotic effect. The plasma was supplied by U S Pharmaceutical Inc. Burbank, Calif. and was prepared in accordance with the regulations of the Division of Biologic Standards of the National Institutes of Health. Additionally the plasma was heated to 60 C for 10 hours. This pasteurization procedure is also the final step in preparation of currently accepted human serum albumin.



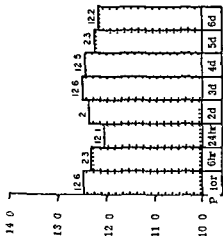
## MEAN HEMATOCRIT LEVELS



## MEAN WBC LEVELS



## MEAN HEMOGLOBIN LEVELS



Time Following Inf

Time Following Infusion

Time Following Infusion

Figure 11.11 of / o / 500 ml / p / t d pool d h m pl m m l f h m gl b l k cyt d h m to t

interval of 3 to 4 weeks elapsed between the infusions. No reactions definitely attributable to the plasma were observed in any instance, in spite of the fact that seven recipients had given histories of allergies to inhalants, foods, and medications. One of these patients received two infusions of plasma. Twenty four hours following the administration of the second infusion which had been given 17 days after the first, edema of the hands was observed, however, inasmuch as the patient reported multiple allergies to penicillin, detergents, and calamine lotion, it is doubtful that this symptom was due to the plasma. This is supported by the demonstration of an identical reaction following the application of calamine lotion 8 days later. Three weeks following the second infusion, he was skin tested with the same plasma and no reaction occurred. A female patient who inadvertently received the plasma very rapidly developed a sensation of lightheadedness, which disappeared as the rate of infusion was reduced. The total volume was administered without other untoward result. No significant changes in blood pressure, pulse rate, or elevation of temperature were recorded. The patients did not complain of any untoward subjective sensations during or following the infusions. In the interest of accuracy and continuity in reporting, most of these infusions were administered and observations were made personally by one of us. To date, 13 to 35 weeks have elapsed since the first and last plasma infusions were administered. Neither jaundice nor other symptoms of hepatitis has occurred in the recipients, though, of course, insufficient time has elapsed to permit a final conclusion about this point. However, inasmuch as this same procedure has been used with success for the sterilization of deliberately contaminated albumin solutions, there is evidence to support the acceptance of the inactivation of the serum hepatitis virus by this process.<sup>9</sup> Figure 1 summarizes peripheral blood observations. Though minor changes in hemoglobin and leukocyte values occurred occasionally, they were not significant. Urinalysis following infusion reflected no proteinuria or increase in proteinuria where it had previously existed and no abnormalities in urinary sediment. Not only were hemorrhagic manifestations absent following plasma administration, but determinations of bleeding time and prothrombin time (one stage) revealed no alterations (fig. 2).

Plasma volumes and total blood volumes were determined in 12 patients (fig. 3). One hour following infusion, there was an average increase in plasma volume of 225 ml and an average increase of blood volume of 330 ml. At 6 hours there was an average increase in plasma volume of 287 ml and in blood volume of 312 ml, and 24 hours following infusion the average increase of plasma volume was 370 ml, and of blood volume was 409 ml. These findings indicate a satisfactory oncotic effect, which is immediate and yet persists for at least 24 hours.

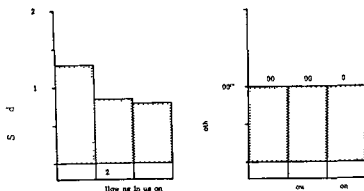


Fig 2 1 flow f f f 500 ml f p t d pl m m  
al f bl d g t m ght and p thr mb t ty l ft

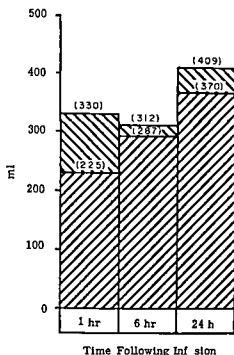


Fig 3 Man ti ff t f 500 ml f  
p t d plasm xp d cr  
pl m a d bl od volum m l l t

The data obtained by electrophoretic separation of serum proteins of the recipients prior to and at 1 6 and 24 hours following plasma infusion are shown in table 1. No statistically significant alterations of albumin alpha alpha beta or gamma globulins were observed after administration of plasma.

TABLE 1 *Effect of infusion of 500 ml of pasteurized human plasma on mean values of electrophoretic partitions of serum proteins of recipients*

Time	Albumin	Alpha <sub>1</sub>	Alpha <sub>2</sub>	Beta	Gamma
Prior	40.1	6.0	14.9	12.3	26.5
1 hr	42.1	5.5	14.5	12.6	26.8
6 hr	40.7	5.9	11.2	13.0	27.1
24 hr	39.0	6.0	14.2	14.4	33.0

### DISCUSSION

Pasteurized plasma used in this study is apparently devoid of any untoward immediate effects. This statement is supported by the absence of subjective and objective evidence of anaphylactoid or other allergic episodes, the absence of symptoms suggestive of significant prejudicial hemodynamic alterations, the failure to demonstrate pyrogenic reactions, the absence of hemorrhagic symptoms or of laboratory evidence of hemorrhagic diatheses, and by the absence of significant alterations of the serum proteins in the recipients of the plasma. From the consideration of these parameters, this preparation appears to be safe. The other experience in 84 patients and the previously reported evidence of the efficacy of pasteurization in the inactivation of the serum hepatitis virus probably assures the long term safety of this preparation inasmuch as the pasteurization of the serum albumin has been satisfactorily accomplished by the same method.

In these clinical trials, data suggest also that this plasma preparation exerts a very satisfactory oncotic effect, with the production of almost a calculated optimal increase in plasma and blood volumes in normal recipients, with maintenance of this effect for at least 24 hours.

On the basis of our experience, it is recommended that more extensive clinical trials with this plasma preparation be conducted in order to substantiate further the usefulness of pasteurized pooled human plasma in the treatment of patients who require blood volume expanders. The logistical superiority of this preparation is obvious.

### SUMMARY

Pooled human plasma, treated by heating to 60°C for 10 hours to inactivate the serum hepatitis virus has been administered 35 times to 30 patients. No immediate untoward consequences were observed. The oncotic effect of this plasma is completely satisfactory.



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- 3 W k l J H J d L ky L M Ph m l gy f lo- d h l l y tem  
bl k d by polyv ylpyr l d (PVP) m ured w h d o- h m ph pha  
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## THE STRANGE LANGUAGE OF PSYCHIATRY

The lack of progress in psychiatry during the past 50 years brings forward a contribution to medical anthropology, may well be attributed to the fact that although psychiatry deals with the obstacles that妨碍 human ability to communicate with his fellow men it has failed to express itself fully. For half a century psychiatry has employed a strange language, verbiage and modulations and obscure. Fortunately it is now pulling itself out of this mire thanks to the uses of physiodynamic and organic psychiatry which speaks the plain language of biology. Thanks to this numerous successes have been achieved during the last five years in the psychochemistry, rape of the field and many more will undoubtedly follow these until in due time the phoenix of mental disease will finally rise and it is clear that this goal demands that psychiatrists set boundaries and restrictions and be more biological and physical in their explorations into the tenebrous world of mental disease.

—FELIX MARTÍ IBÁÑEZ M D

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# PERCUTANEOUS SPLENOPORTOGRAPHY IN PORTAL HYPERTENSION

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**P**ORTAL HYPERTENSION may arise from obstruction of veins outside the liver, or from intrahepatic causes. Surgical relief by means of a portal vein to vena cava shunt is indicated in cases where esophageal varices develop. These shunts are more satisfactory than splenorenal shunts, but can not be performed if the portal vein is thrombosed or has undergone cavernous transformation, or if certain other circumstances exist. Roentgenographic visualization of the portal vein and its tributaries is important in distinguishing the site of obstruction so that the proper operative procedure may be selected. Since July 1957 percutaneous splenoportography at this hospital has been a part of the preoperative study of patients with portal hypertension. We wish to report our experience with this diagnostic method.

Patients suspected of having portal hypertension were carefully investigated by history taking, physical examination, and indicated laboratory tests as well as by liver biopsy and esophagoscopy. Prolongation of bleeding or clotting times, prothrombin time below 40 per cent of normal, or platelet count below 60,000 were accepted as contraindications for splenoportography.

## TECHNIC

Seventy five milligrams of meperidine hydrochloride (Demerol) is given intravenously together with a 1 ml test dose of the contrast material sodium diatrizoate, (50 per cent Hypaque) after the patient is positioned on the radiographic table. Epinephrine and Nalline Hydrochloride (brand of nalorphine hydrochloride) should be available to combat adverse reactions. The patient is instructed in breath holding at this time. By percussion and palpation of the spleen, a site for insertion of the needle is selected. This is usually in the left midaxillary or posterior-axillary line at the eighth or ninth intercostal space. After skin preparation and infiltration with a local anesthetic has been

accomplished the patient is told to hold his breath in mid inspiration. A No. 18 spinal needle is inserted into the spleen. Slight resistance often can be detected as the needle penetrates the capsule. A flow of venous blood from the needle after the stylet is withdrawn indicates that the needle is within the splenic substance. It is important that the patient not breathe while the needle is being manipulated; otherwise the splenic capsule might be torn. Once the needle is within the spleen and released by the operator, shallow breathing can be resumed. Splenic pressure is measured with a saline solution filled manometer connected to the needle by a flexible polyethylene tube. This permits measurements to be made while the patient breathes. Values above 900 mm of saline solution are considered to be abnormally elevated. A Valsalva maneuver will increase the pressure and confirm the correct placement of the needle. The splenoportogram is made by injecting 25 ml of sodium diatrizoate (50 per cent Hypaque) rapidly into the spleen. This is accomplished through a polyethylene tube which connects the syringe to the needle. The needle is removed from the spleen when all of the contrast material has been injected. Serial x-ray exposures are made over a 10 second period using a Schönander biplane film changer. If only a single roentgenogram can be taken, the exposure is made just before the last few milliliters of contrast material are injected. After the procedure the patient is not permitted to move but is lifted onto a litter, returned to the ward, and lifted into bed. The patient is then kept flat in bed for six hours after which he can sit up. He must, however, remain in bed for 24 hours. Pulse rate and blood pressure are measured frequently for the first six hours.

### RESULTS

Thirty splenoportograms were performed in 23 patients in the period from July 1957 through April 1958. There were 19 males and 4 females in this series. The average age was 44 years and the age range was 7 to 68 years. Diagnoses included portal cirrhosis, 10 patients; postnecrotic cirrhosis, 5 patients; biliary cirrhosis, 1 patient; portal vein thrombosis, 2 patients; hemachromatosis, 1 patient; fibrocystic disease, 1 patient; hemangioma of liver, 1 patient; and portal cirrhosis with hepatoma, 2 patients. Portal hypertension was present to some degree in all but two of the patients, and ascites had occurred in 11. Esophageal varices were present in all but two patients, and 15 had experienced upper gastrointestinal hemorrhage. Seventeen of these patients had had previous or subsequent surgical shunt procedures to relieve portal hypertension. Only four of this number were splenorenal. The remainder were end-to-side portacaval anastomoses.

The success of splenoportography was evaluated considering adequacy of radiographic visualization and accuracy of splenic

pulp pressure measurement, as gaged by comparative pressure measurement at time of surgical intervention. Adequate radiographic demonstration of the portal venous system was obtained in 20 of the 23 patients (87 per cent), however, in only 23 of 30 procedures (76.6 per cent) were satisfactory results obtained. The main causes of failure were about equally divided between subcapsular collection of dye, failure to inject the dye into the spleen, and technical failure of the Schönander machine. Pressure measurements were successful and reasonably accurate in 20 of 22 patients and in 25 of 29 attempts. This figure includes one patient in whom three consecutive attempts were unsatisfactory. Thus satisfactory pressure measurements were obtained in 91 per cent of the patients and in 86 per cent of the attempts. Considering these two sets of data collectively, it may be said that in only two procedures (6.6 per cent) in the same patient was there absolutely no information gained by splenoportography. This same patient had a third successful splenoportogram, thus the procedure was successfully accomplished in all patients.

There was one complication—one patient bled intraperitoneally sufficiently to justify a 1 liter blood transfusion. He had been unable to remain aperiodic during the procedure because of ascites and right hydrothorax. Several patients required one injection of meperidine for right upper quadrant or right shoulder pain.

### CASE REPORTS

Case 1. Massive hematemesis caused this 38-year-old Caucasian male medical technician to be hospitalized in March 1956. In January 1956 he had had unexplained melena. There was a past history of gout, prolonged obesity, and renal calculi, but none of hepatitis, excessive alcohol intake, dietary deficiency, or exposure to hepatotoxic agents.

Physical examination revealed obesity and hepatosplenomegaly, but no spider angiomas, alopecia, telangiectasis, palmar erythema, ascites, or other evidence of chronic liver disease.

Laboratory studies showed a mild leukopenia, thrombocytopenia, and anemia. There was 30 per cent ulfthomoptimalin in retention in 45 minutes. Liver biopsy showed evidence of focal necrotic cirrhosis. Large esophageal varices were seen on esophagoscopy was performed.

A portacaval shunt was performed for the patient. The patient had a good response to the shunt and remained free of gastrointestinal bleeding. He was again hospitalized for the same reason. At the time of the second hospitalization, a second splenoportogram was performed. The results of the second splenoportogram were as follows:



surgical shunt, splenoptography prevented this patient from undergoing an additional, useless, major surgical procedure

**Case 2** This 15 year-old girl was the only one of five children to survive more than one year. Her siblings died of intestinal obstruction and/or pneumonia. Since early life she had experienced frequent upper respiratory infections and was accustomed to passing six to eight yellow frothy bulky foul smelling stools a day. Pancreatic insufficiency was diagnosed at the age of five. The patient has been treated with pancreatin granules and a low fat diet ever since this diagnosis was established. Steatorrhea continued. At age 11 she developed a productive cough, dyspnea on exertion and roentgenographic evidence of biapical pulmonary infiltrates occurred. Early clubbing of the fingers was noted and treatment with antibiotics and various expectorants was initiated without symptomatic improvement. At age 14 the patient noted the gradual onset of easy fatigability, general weakness and malaise. In December 1956 splenomegaly was noted and her hemoglobin level was 5.5 grams per 100 ml. Upper gastrointestinal series, barium enema and liver function studies were normal. Transfusions were given and she returned to school. In August 1957 an episode of massive hematemesis occurred which prompted rehospitalization and an eventual transfer to this hospital on 15 October.

Physical examination revealed a small but well-developed and well-nourished 15 year-old white girl with a blood pressure of 110/70 mm Hg. There was a slight increase in thoracic anteroposterior diameter, hyperresonance of the lung fields and a lower thoracic outward flare. Splenomegaly, clubbing of the fingers and questionable ascites were the only other positive findings. The liver was normal in size. There was no icterus, spider angiomas, telangiectasis, hair loss or palmar or plantar erythema.

Laboratory studies showed anemia, thrombocytopenia and leukopenia. A chromium<sup>51</sup> red cell survival study demonstrated evidence of a moderately severe hemolytic process, presumably from hypersplenism. Bone marrow aspiration showed erythroid hyperplasia. Stool fats were consistently well above normal limits and serum cholesterol was low (123 mg per 100 ml). Stools were negative for trypsin activity. Roentgenograms of the chest and pulmonary function studies indicated the presence of pulmonary emphysema and fibrosis. Liver function studies including serum bilirubin, thymol turbidity, cephalin cholesterol flocculation, alkaline phosphatase, sulfo-bromophthalein sodium retention, total serum proteins and albumin globulin ratio were all normal.

On 26 October esophagoscopy revealed moderate sized varices extending the length of the esophagus. Splenoptography was performed four days later and the splenic pulp pressure was measured as 440 mm of saline solution. Parent splenic and portal veins were visualized. The patient had a second bout of hemorrhage from varices which precipitated further ascites, icterus and liver function ab-



sized varices, and no hepatomegaly or hepatic dysfunction. Patent splenic and portal veins were noted by splenoportography thus assuring the surgeon of the presence of adequate sized veins with which to construct a portacaval anastomosis. The success of the portacaval anastomosis in relieving portal hypertension was well demonstrated by the repetition of splenoportography about three weeks postoperatively.

**Case 3** This 7 year-old boy was adopted by American parents in Germany at the age of two and one half years. Following adoption hepatosplenomegaly was noted and despite a rather detailed medical evaluation a specific diagnosis could not be made. He remained asymptomatic and growth and development progressed normally during the next five years although repeated medical check ups usually demonstrated splenomegaly. Seven days before admission to a hospital there occurred slight fever, general malaise and a sore throat followed by vague abdominal pains and failure of the patient to have his usual daily stool. The next day after a laxative had been given a black tarry stool was passed. The abdominal pains, constipation and passage of tarry stools continued for six days before medical attention was sought. Because of rather marked anemia (hemoglobin 5 grams per 100 ml) the patient was admitted to a hospital on 11 December 1957 given a transfusion and transferred to this hospital two days later.

Physical examination demonstrated signs of anemia, slight hepatomegaly, moderate splenomegaly, abdominal distention with some ascites and a tarry stool in the rectum.

Laboratory data included a hemoglobin of 7 grams per 100 ml, hematocrit of 20 ml per 100 ml, sulfobromophthalein sodium retention of 20 per cent at 45 minutes and a total serum protein of 4.9 grams per 100 ml (albumin 2.7 grams per 100 ml). Total serum bilirubin, alkaline phosphatase, cephalin-cholesterol flocculation, thymol turbidity and serum electrolytes were all within normal limits. Radiographic study of the esophagus demonstrated varices.

During the first two weeks of hospitalization the patient continued to bleed intermittently from esophageal varices and 3,500 ml of blood replacement was necessary. Bleeding had stopped by 25 December 1957. Splenoportography was performed on 30 December and a cavernous transformation of the portal vein was found (figs. 3 and 4). Splenic pulp pressure was 460 mm of saline solution. Because of this evidence of portal hypertension secondary to extrahepatic portal vein obstruction a splenorenal anastomosis was performed immediately after splenoportography. Pressure within the splenic vein was determined at operation to be 380 mm of saline and this fell to 220 mm of saline after the shunt was completed.

Convalescence was uneventful and the patient returned home 12 days after surgical intervention. He has had no recurrent hemorrhage to this date.





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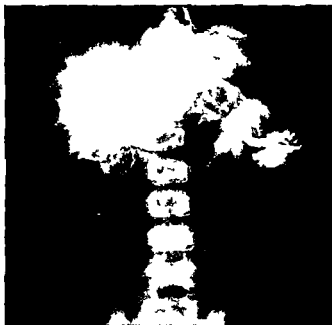


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*Comment* Again, it is noteworthy that only by splenoportography was the diagnosis of extrahepatic portal vein obstruction proved. The surgeon was thus directed to the proper operation after noting a patent, satisfactory splenic vein upon roentgenographic examination.

**Case 4** A 46 year old man began to use alcohol excessively in 1952 and was found to have liver disease in 1954 when he was hospitalized following a grand mal seizure. Development of erythematous weeping lesions of his ears and face led to his hospitalization in 1957 after treatment with ammoniated mercury and cortisone ointment had failed. Anorexia, weight loss and dyspnea had occurred during the month prior to hospitalization.

On admission to this hospital the patient's temperature was 101°F, his respirations were 28 per minute and he was dyspneic and acutely ill. Erythematous scaling lesions were present on his ears and over the beard area of his face. He had scleral icterus and his liver was felt 5 cm below the right costal margin. A grade 2 systolic murmur was heard over the precordium.

His hemoglobin was 9.8 grams per 100 ml, hematocrit 30 mg per 100 ml, white blood cell count 7,700 per  $\mu$ l, total serum bilirubin 4.5 mg per 100 ml, thymol turbidity 2 units, cephalin-cholesterol flocculation 3 plus, sulfobromophthalein sodium 50 per cent retention in 45 minutes, serum albumin 2.5 grams per 100 ml and serum globulin 3.6 grams per 100 ml. His stool was 3 plus for occult blood. Several lupus erythematosus preparations were negative.

The patient gradually became afebrile over the first two weeks. His stools became free of occult blood and his hemoglobin became normal. Cardiac disease could not be demonstrated. Radiographic studies while swallowing barium and esophagoscopy showed esophageal varices and a liver biopsy demonstrated Laennec's cirrhosis. Skin biopsy of the face revealed discoid lupus erythematosus which disappeared with chloroquine therapy leaving residual atrophy and vitiligo. A splenoportogram showed a well visualized splenic vein running a somewhat tortuous course 8 to 9 mm wide and a portal vein 7 cm long and 6 to 7 mm wide (fig. 5). Splenic pulp pressure was 226 mm saline solution. A repeat splenoportogram demonstrated the same configurations and a splenic pulp pressure of 170 mm of saline. Because the portal and splenic veins were not dilated, and the portal pressure was within normal limits, no attempt was made to perform a portacaval shunt and the patient was discharged to duty. At the time of discharge his total serum bilirubin was 0.8 mg per 100 ml, thymol turbidity 1 unit, cephalin-cholesterol flocculation negative, alkaline phosphatase 65 Bodansky units and sulfobromophthalein sodium 20 per cent retention in 45 minutes.

*Comment* Although this patient had all of the findings of Laennec's cirrhosis with associated esophageal varices, and appeared to have had portal hypertension at one time, splenic

pulp pressures on two separate occasions were normal. This would seem to indicate that natural collaterals sufficient to relieve his portal hypertension had developed.



Fig 5 (as 4) Splenophtogram showing portal and postportal anastomosis. The flow of blood from the portal system into the coronary and hepatic arteries is demonstrated.

C 5 This 40 year old nulliparous woman with significant alcoholic history had a tooth extracted in September 1956. Local procaine anesthesia was used. During November and December she had anorexia and fatigue. She was admitted to an orthopedic hospital in January 1957 and was found to have a slightly tender liver enlarged 7 cm below the right costal margin, spider angiomas, and sclerotic icterus. Her height, serum bilirubin was 9.7 mg per 100 ml, albumin 3.0 gams per 100 ml, and serum globulin 4.5 gram per 100 ml. During hospitalization ascites developed and she was treated with mercuric diuretic, two paracenteses, several units of sodium poor human albumin, and a low sodium diet. It did not achieve a high-calorie diet and

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# PERCUTANEOUS SPLENOPORTOCALYSIS

supplemental vitamins were given. Initially her hemoglobin was 10 grams per 100 ml, but this rose with iron therapy. In February she developed some fibrosis but followed as an outpatient at this hospital. By August bromothalein sodium retention was 22 per cent. In September after 10 days of treatment associated with intermittent upper abdominal pain she was admitted to this hospital.

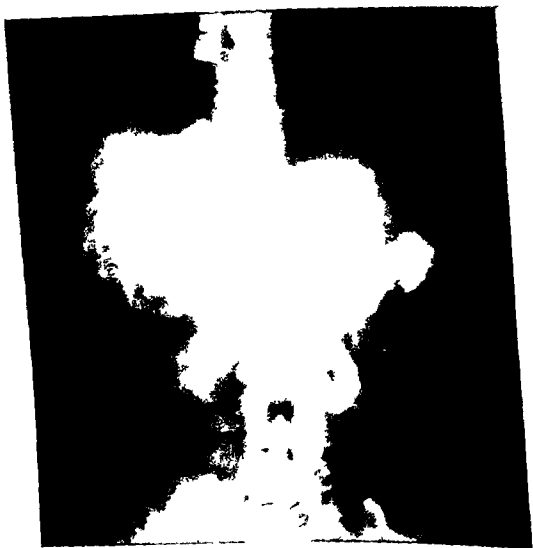


Figure 6 (case 5) The splenic and portal vein are dilated. Right and left branches of the portal vein are dominant at d.

Physical examination at this time revealed marked pallor, tachycardia, spider angiomas, scleral icterus, and a liver enlarged to 8 cm below the right costal margin. Laboratory studies on admission revealed a cephalic-cholesterol flocculation of 2 plus, normal thyroid turbidity and alkaline phosphatase activity of 2.6 grams per 100 ml and a globulin of 2.9 g per 100 ml. A total serum bilirubin of 3.6 mg per 100 ml and a bromothalein sodium retention of 41 per cent.

The patient continued to bleed during the first four days of hospitalization passing bright red blood on the fourth day with her hemoglobin falling to 6.0 grams per 100 ml. She required five pints of blood during this period.

Bleeding was controlled with a Sengstaken-Blakemore tube kept in place for three days. Esophagoscopy with the tube in place showed large esophageal varices. Roentgenograms of the gastrointestinal tract did not reveal any other lesions. A liver biopsy showed portal cirrhosis with minimal fatty infiltration. Splenoportogram showed a very small splenic and portal vein but finely ramifying collateral vessels were seen to arise from the coronary vein (fig. 6). The inferior mesenteric vein was small, tortuous, and displaced. Gastric and esophageal varices were visualized. Splenic pressure was 460 mm of saline solution. Three weeks later a portacaval shunt was performed. The portal vein was only 7 mm wide and the shunt was accomplished with difficulty. The portal pressure of 420 mm of saline only dropped to 350 mm. The patient tolerated the procedure well but two weeks later ascites developed following massive hemorrhage. The bleeding was controlled by use of the Sengstaken-Blakemore tube.

*Comment.* In this patient who was rather early in the course of her illness, the portal system dilatation and large collateral network usually associated with this degree of portal hypertension had not yet developed. A splenorenal anastomosis was considered but thought contraindicated inasmuch as the splenic vein also was small and the majority of this patient's collaterals would be destroyed by such a procedure. Portacaval shunt did not produce sufficient reduction of portal pressure to prevent subsequent hemorrhage. Another attempt at surgical treatment of the varices seems indicated.

**Case 6.** This 46-year-old man with history of alcoholism was found to have an enlarged liver in 1948. Massive hematemesis requiring transfusion with 11 pints of blood occurred in December 1955. Esophagoscopy showed esophageal varices and a liver biopsy showed Lennec cirrhosis. After a second episode of hematemesis in February 1956, a portacaval shunt was performed at this hospital. Esophagoscopy in December 1956 revealed no varices. In March 1957 he had six tarry stools and four pints of blood were given. Small varices were found on esophagoscopy. Progressively worsening dyspepsia and fatigue and the passage of two tarry stools led to his readmission in July 1957.

Physical examination revealed marked pallor, a systolic precordial murmur, tachycardia, a large lump 7 cm below the right costal margin, many spider angiomas, marked palmar erythema, and 2+ ankle edema.

Laboratory data revealed a hemoglobin of 4.1 grams per 100 ml, white with two pints of blood and nutritional edema (imfe) rose steadily to 9.5 gram per 100 ml with only one inter-

vening episode of melena. Total serum bilirubin was 2.8 mg per 100 ml and sulfobromophthalein sodium retention was 22 per cent. Serum albumin was 2.1 grams per 100 ml, serum globulin 3.5 grams per 100 ml, cephalin-cholesterol flocculation 3 plus in 48 hours, thymol turbidity negative, alkaline phosphatase 7.6 Bodansky units, and prothrombin time ranged from 45 to 65 per cent of normal. Live biopsy again showed Laennec's cirrhosis. Radioscopy and radioeraphy of the gastrointestinal tract showed no other lesions.

Esophagoscopy showed only minimal esophageal varices. No evidence of a hemolytic process could be found, and the anemia was ascribed to chronic blood loss. A splenoportogram in August showed good visualization of the splenic and portal veins with good filling of the inferior vena cava and no evidence of closure of the shunt (fig. 7). Splenic pulp pressure was 250 mm of saline. The patient continued to drink alcohol.



Figure 7 (case 6) Patent portacaval shunt in a patient with esophageal varices and gastrointestinal bleeding 18 months after operation.

He returned to this hospital in December with marked ascites, icterus, bleeding esophageal varices, hypoalbuminemia, and hepatic coma, which eventually responded to vigorous therapy. Although he remains anemic, icteric, and collects fluid readily, he is again semi-

ambulatory and shows steady low improvement on an outpatient regimen of sodium restrict protein restriction (because of meat intoxication) diuretics salt poor human albumin infusions and parenteral iron therapy

*Comment* This patient's sudden downhill course could have been precipitated by either a thrombosis of the portacaval shunt with recurrent portal hypertension and bleeding esophageal varices or by progressive hepatic insufficiency hastened by gastrointestinal hemorrhage from some site other than esophageal varices Splenoportography with manometry proved the portal venous pressure to be normal Further surgical efforts to form vascular shunts do not seem indicated

### DISCUSSION

Radiographic visualization of the portal venous system by the injection of contrast material into a suitable vessel at the time of laparotomy has been performed since 1945 This technic not only prolongs operating time and fails to provide for multiple serial films but most important it requires the surgeon to make his incision without knowing definitely on which side of the abdomen he will be operating Portal vein visualization following intrasplenic injection at laparotomy was reported in 1951 by Pereira The percutaneous approach was used in experimental animals by Abeatici and Campi and in humans by Leeger and by Boulyin and associates Although the early reports came from continental Europe and England Blalock in 1947 noted portal vein visualization by accident when he was injecting a sinus tract which entered the spleen This led to the clinical use of percutaneous splenoportography at Johns Hopkins Hospital as early as 1949 but the results were not published until 1953 Many persons contributed technical improvements and in 1954 Atkinson and Sherlock<sup>1</sup> demonstrated that manometric measurements in the splenic pulp gave an accurate appraisal of the portal vein pressure It is now possible to detect portal hypertension quantitate it radiographically demonstrate its effect and occasionally to determine its cause

Other approaches to the portal venous system have been attempted Percutaneous injection of contrast substance into an intrahepatic branch of the portal vein has been performed 144 times in 73 patients without serious complications<sup>1, 2</sup> The main portal vein splenic vein and collaterals are not demonstrated by this technic The hepatic arterial and intrahepatic portal venous system also can be visualized by abdominal aortography Neither of these methods gives quite as much information as percutaneous splenoportography and both seem somewhat more hazardous

From 1953 through 1956 articles began appearing in the American literature and the technic spread slowly throughout

this country Rodriguez, Gardner, and Diaz Bonnet,<sup>16</sup> O'Sullivan and Evans,<sup>17</sup> Cooper and associates,<sup>18</sup> as well as Bahnson and co workers<sup>11</sup> were responsible for this spread of enthusiasm. Further larger series of patients have been reported during the past year, and additional indications for splenoportography continue to appear.

DeWeese and associates<sup>1</sup> reported 134 splenoportograms on 120 patients in which 84.3 per cent were successfully completed. Serious splenic hemorrhage occurred in only one patient. Surgical intervention was not required. The prime value was in the evaluation of portal hypertension, the evaluation of portocaval shunts, and occasionally as an aid in the diagnosis of hepatic and pancreatic tumors. In only 17 cases were splenic pressures determined.

Turner, Sherlock, and Steiner<sup>2</sup> reported their results in the 126 venograms in 109 patients. Fourteen of these were failures. Splenic pulp pressures were taken as part of the procedure. Primary indications were gastrointestinal hemorrhage with suspected portal hypertension, undiagnosed hepatomegaly and splenomegaly, neuropsychiatric changes in patients with liver disease, suspected hepatic tumor, ascites of unknown cause, and postoperative investigation of portocaval anastomosis. A few patients were seen with large collateral vessels but without increased splenic pulp pressure. Occasionally splenic pulp hypertension was noted without the presence of varices or other collaterals. Patients were followed in whom collaterals developed with a consequent loss of portal hypertension but with the occurrence of varices. Thus it was thought that bleeding esophageal varices could occur in the absence of portal hypertension and were not related solely to the latter. During 1957, Gilsanz, Vergara, and Estella<sup>21</sup> used percutaneous splenoportography in differentiating constrictive pericarditis from congestive hepatomegaly of other cardiac origin. The spleen to lung circulation time was measured with ether injected into the spleen in the same manner as, and compared with, the arm to lung circulation time. In two patients with constrictive pericarditis, there appeared an increased spleen lung circulation time which was out of proportion to the arm lung time, and with a markedly decreased visualization of the portal vein ramifications. These findings returned to normal after pericardiectomy.

While not a completely innocuous procedure the relative safety of splenoportography becomes better documented each year. The danger of splenic hemorrhage remains, however, and 300 to 400 ml of blood in the peritoneal cavity has been noted on several occasions in patients coming to laparotomy for other reasons. Rarely has transfusion been necessary for clinical blood loss and in only two reported cases<sup>22</sup> was emergency splenectomy required because of hemorrhage.



The success of splenoportography in producing adequate visualization of the portal venous system is well documented in the more recent and larger series. In the combined reports of DeWeese and associates and Turner and co workers adequate visualization was obtained in 295 of 260 procedures (86.5 per cent). This excellent result demonstrates what may be expected from experienced operators. The main reasons for failure were (1) the inability to inject the dye into the spleen because of faulty needle placement (2) subcapsular infiltration of the dye even though the dye was injected into the spleen and (3) technical failure of the radiographic equipment.

It is agreed that these patients should be hospitalized when the procedure is performed and that a basic hematologic work up including bleeding time clotting time prothrombin time platelet count and complete hemogram be performed prior to splenoportography. When a bleeding tendency is not correctable splenoportography should be delayed until immediately preoperatively any splenic bleeding can then be controlled while the abdomen is open.

It is our belief that splenoportography should be performed (1) for the determination and measurement of portal hypertension (2) to allow preoperative selection of the proper surgical shunt operation (3) to properly evaluate the shunt function at later dates and (4) as a diagnostic aid in the evaluation of hepatic tumors obscure splenomegaly and ascites congenital portal venous system anomalies portal vein thrombosis and gastrointestinal hemorrhage.

### SUMMARY

Percutaneous splenoportography combined with measurement of the hydrostatic pressure in the spleen is safe simple and useful in evaluating the anatomy and function of the portal venous system. It provides an estimate of the degree of portal hypertension and distinguishes between those patients who will benefit from a portacaval shunt and those who require a spleno-renal shunt. Patency of portacaval shunts can be determined by its use.

Twenty three patients were subjected to 30 such procedures. Satisfactory x ray films were obtained for 20 patients and pressure determinations were satisfactory in 20 patients. Useful information was obtained concerning each patient examined.

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# RADIOGRAPHIC DIAGNOSIS OF ATHEROSCLEROSIS

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**A**THEROSCLEROSIS is among those pathologic conditions referred to as the degenerative diseases. It is not however limited in its occurrence to the twilight years of life. The coronary arteries of 300 American casualties of the Korean Conflict showed gross evidence of atherosclerosis ranging from minimal change to complete occlusion in 77.3 per cent. The average age of these casualties was 22.1 years. The young coronary victim has been well documented clinically and is familiar to all physicians. Atherosclerotic occlusion of a large vessel such as the aorta may occur early in the fourth decade of life.

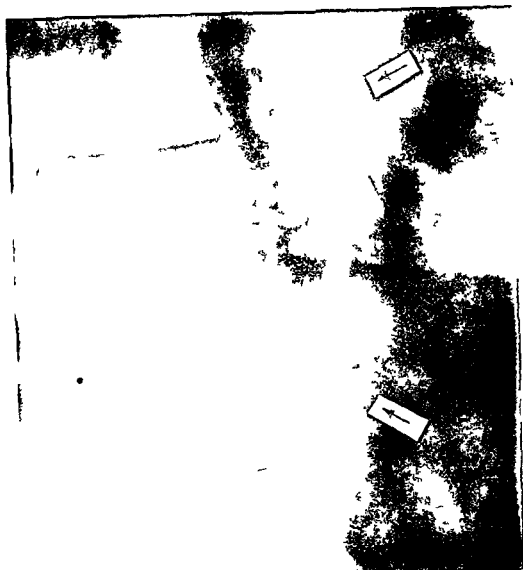
Occlusive vascular disease is being intensively studied in many areas of investigation. Unfortunately much of the knowledge thus accumulated is not yet thoroughly correlated for clinical application. The extent to which diet, familial tendency, exercise, habits, stress, and other factors interrelate in the development of atherosclerosis is still controversial. The extensive investigation in progress undoubtedly will eventually provide many answers as to the future anticipation, diagnosis, and control of the disease. The opportunity to discover cases of unsuspected or subclinical atherosclerosis by incidental roentgen finding is most appealing and of tremendous potential benefit to the patient.

## ROENTGEN DIAGNOSIS

The radiographic demonstration of atherosclerotic calcification is as conclusive in the diagnosis of the disease as is biopsy. The condition is rendered roentgen demonstrable by deposition of calcium salts near the base of atheromata and deep in the intima where the process began. Typically atherosclerotic calcification is dense, patchy, and plaque-like (fig 1). These plaques may vary in appearance from small rounded flecks of calcium to large, irregular calcific densities up to 2 cm in size.

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F m U S A F H p l P k Air F B C l f Th uth w  
g d U S A F H p l L k l d A F B T



*Figure 1 Typical atherosclerotic calcification of the abdominal aorta seen on a lateral view of the lumbo-sacral spine*

Atheromatous calcification must be differentiated from the calcification of muscular arteries seen in medial (Monckeberg's) sclerosis (fig 2). This latter calcification is typified by multiple concentric—but usually incomplete—rings or sheets of calcific density producing a trachea like or gooseneck appearance. The radiographic demonstration of medial sclerosis is not significant in our present terms of reference as the disease is not occlusive. Medial calcification may, however, obscure coexistent atheromatous plaques.<sup>2</sup>

Atherosclerotic plaques must also be differentiated by location and appearance from calcification resulting from tumor calculus, inflammation, and physiologic processes in adjacent soft tissues.

Calcified atheromatous plaques are most commonly visualized in the abdominal aorta and its branches, but may be demonstrated



have radiographically demonstrable arterial calcification in some region of the body.<sup>4</sup> Sixty seven per cent of males with clinically evident peripheral atherosclerosis will have calcium in the atheromatous lesions.<sup>5</sup> In 21 men with proven occlusive coronary disease,<sup>6</sup> atheromatous calcification of the aorta or great vessels or both was visualized on films of the abdomen in 28.6 per cent. In a control series, the incidence was only 9.1 per cent (table 1).

TABLE 1 Age of patients and incidence of roentgen-demonstrable atherosclerosis

Group	Number of patients	Age range	Average age in years	Roentgen-demonstrable atherosclerosis in the abdomen	Incidence of roentgen-demonstrable atherosclerosis
Patients with coronary heart disease	21	35 to 44 inclusive	39.2	6	28.6 per cent
Neurosurgical patients with discogenic disease	22	35 to 44 inclusive	39	2	9.1 per cent

### CLINICAL APPLICATION

The finding of arterial calcification in younger military personnel is of obvious importance in provoking further study. Its demonstration in individuals with critical or high performance job requirements would particularly demand extensive investigation and close follow up. Because there is correlation between radiographically demonstrable atheromatous plaques and occlusive disease, a definite indication of atheroma should stimulate efforts toward early diagnosis of atherosclerosis.

In patients with clinically apparent disease, the observation of arterial calcification may provide the initial impetus toward definitive diagnosis. Carotid or cerebral arterial calcification may suggest the cause of transient neurologic disturbance (fig. 3). When examining the intravenous pyelogram one may note calcified hypogastric arteries as the significant diagnostic clue to the patient's difficulty. The physician who looks beyond the spine may discover calcification indicating vascular insufficiency as the cause of hip or leg pain (fig. 1). Each x-ray examination affords opportunity to diagnose the presence of atherosclerosis with certainty.

Thus the "radiologist"—be he such by training, designation, or default—has a responsibility to point out atherosclerosis



*Fig 3 Atherosclerotic plaque the carotid artery*

and its possible significance whenever encountered. Many cases may be detected before severe complications or even clinical symptoms arise.

### INTERPRETATION

As atherosclerosis is a degenerative disease, determination of the age at which arterial plaques represent a significant radiographic finding is difficult and varies with the patient and the problem involved. It is our practice to make the finding of atherosclerotic disease the high light of the radiographic report in patients under 40 years of age. In the 40 to 50 year age group, the observation is given prominence in the report. In patients more than 50 years of age, the observation is presented as an incidental finding unless it is related to the condition that prompted the examination.

We do not propose the radiographic demonstration of atherosclerotic plaques as the final answer in early detection of atherosclerosis, but believe that its value as an additional investigative stimulant or diagnostic clue has been understressed and deserves emphasis.

We believe that roentgen demonstrable atherosclerosis is a significant and poorly explored avenue in the overall study of vascular disease. Such a concept is the result of impressions

gained from clinical observations small control and clinical groups, and current literature. Admittedly, there are questions that remain unanswered at the present time because of lack of data—the prognostic significance of a single lesion, correlation and time relationship between demonstration of a lesion and subsequent vascular accident, et cetera. It is believed that the paucity of such data in the literature is related, first, to lack of investigation of this area, and second, to inherent difficulty in collecting large series of early atherosclerotic patients and obtaining long follow up. It is our hope to stimulate awareness of the fact that radiographic diagnosis in atherosclerosis is not limited to study of the intrathoracic structures, and to emphasize the implications of other radiographic findings in the disease.

### SUMMARY

The radiographic demonstration of atherosclerotic vascular calcification is always significant. As an indication of serious generalized disease, it is a sign that should be carefully sought on every roentgenologic examination. Its detection by radiography provides an excellent opportunity to study and treat subclinically affected individuals prior to the evolution of severe complications. In patients with clinical manifestations, the finding of atherosclerotic calcification may supply important diagnostic clues.

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**ACKNOWLEDGMENT** This paper represents one area of a broad investigation of cardiovascular disease conducted at this hospital under the direction of Col James H. Hammond, USAF (MC). The authors are grateful to Dr Hammond for his encouragement and assistance.

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# THE DIAGNOSIS OF VIRAL ENCEPHALOMYELITIS

JAMES E BANTA L t t C mm d r MC USN

**N**EUROTROPIC virus infection of the central nervous system usually results in a diffuse meningoencephalitis. This is often termed aseptic meningoencephalitis because the spinal fluid is not purulent and bacteria are not recoverable. Such cases may present problems in differential diagnosis. When it is suspected that the illness may be caused by a virus, the attending physician assumes a responsibility for identification of the specific etiologic agent inasmuch as most virus diseases involve groups of people and are therefore of public health significance.

Although specific diagnosis of virus diseases is not an easy task, advances in recent years have accelerated the procedure to the point where it now offers some assistance in differential diagnoses of the more acute disorders of the central nervous system. It is important that the physician understands the potentialities and limitations of the virology laboratory and keeps abreast of new developments in the field if he is to obtain maximum help. Teamwork between the clinician and the virology laboratory is essential. This article reviews virological diagnostic techniques in current use, outlines the clinical material needed, and briefly discusses the value of the several techniques in various virus infections.

## CLINICAL MANIFESTATIONS

Since neurotropic virus infections tend to cause a diffuse meningoencephalitis, those manifestations suggestive of such diffuse involvement are of primary concern to the virologist. Symptoms and signs are headache, lethargy, chilliness, anorexia, nausea and vomiting, muscle pain, visual disturbances, sensory change, pyrexia, irritability, nuchal rigidity, somnolence, and abnormal reflexes.

If the clinical work up of the patient and analysis of the cerebrospinal fluid indicate a diagnosis of aseptic meningoence

phalitis, then final etiologic diagnosis must be sought by the virology laboratory

### POSSIBLE ETIOLOGIC AGENTS

The number of infectious agents capable of producing aseptic meningoencephalitis is extensive, and must be considered by the virologist who wishes to establish a diagnosis <sup>4-6</sup> Infectious agents considered to be possible causes of aseptic meningoencephalitis include

#### Non arthropod borne encephalitides

- 1 Rabies
- 2 Lymphocytic choriomeningitis
- 3 Herpes simplex
- 4 Herpes zoster
- 5 Mumps
- 6 Measles
- 7 Infectious mononucleosis (?)

#### Enteroviruses

- 1 Poliomyelitis
- 2 Coxsackie—Group A
- 3 Coxsackie—Group B
- 4 Echo ( orphan ) viruses

#### Arthropod borne viruses

- 1 Japanese B encephalitis
- 2 Murray Valley encephalitis
- 3 Russian spring summer encephalitis
- 4 St Louis encephalitis
- 5 West Nile virus
- 6 Sindbis virus
- 7 Equine encephalomyelitis
  - a Western
  - b Eastern
  - c Venezuelan

#### Miscellaneous African Viruses

- 1 Semliki Forest
- 2 Ntaya
- 3 Uganda S
- 4 Bwamba
- 5 Zila
- 6 Bunyamwera, et cetera

#### Miscellaneous Infections

- 1 Leptospirosis
- 2 Toxoplasmosis

Epidemiologic circumstance will enable the laboratory to rule out a number of these agents depending on the season and the geographic origin. In this age of rapid transportation however no agent should be excluded without consideration.

### VIROLOGIC DIAGNOSTIC METHODS

The proper collection and preservation of specimens for laboratory examination is of paramount importance and if incorrectly done may preclude a diagnosis. Specimens are obtained for three principal purposes (1) for primary isolation of the viral agent causing the infection (2) for demonstration of a specific response in antibody titer and (3) for histopathologic examination.

Inasmuch as immunologic examination of the blood serum is the most readily available and most satisfactory technic for establishing a diagnosis it will be considered first. Blood must be obtained from the acutely ill patient as early as possible. A second sample of blood is obtained about 10 to 21 days after the onset of the disease and at least 8 days after the first sample. The blood must be obtained under sterile conditions and permitted to clot at room temperature. After clotting the specimen should be centrifuged and the serum separated and frozen. The frozen paired sera should be sent to the laboratory under refrigeration.

A fourfold rise in the titer of specific antibody in the second specimen is highly indicative of infection and in most instances will establish a diagnosis. The virologist must have adequate clinical data in order to interpret the results properly therefore a record of the case work up should accompany each specimen.

There are three principal immunologic tests available for demonstrating the presence of specific antibodies (1) complement fixation (2) hemagglutination inhibition and (3) neutralization.

#### Complement Fixation

The complement fixation test depends upon the ability of a virus antigen and serum antibody to fix complement thereby preventing fixation of the complement by hemolysin and sheep erythrocytes. The greater the dilution of serum which will prevent hemolysis of the sheep erythrocytes, the higher the titer of antibody present. As a rule the complement fixing antibody has a broader antigenic structure than the neutralizing antibody. The complement fixation test therefore is usually less specific than the neutralization test. Except in lymphocytic choriomeningitis the complement fixation test becomes positive later than the neutralization test and reverts to negative much sooner than the neutralization test. Hence a serum specimen which

possesses a high complement fixing antibody titer is indicative, as a rule, of a recent infection and may have diagnostic significance

### Hemagglutination Inhibition

Hallauers' first reported hemagglutination of erythrocytes by neurotropic viruses in 1947. The subsequent work of Casals and Brown<sup>4</sup> established hemagglutination and hemagglutination inhibition as valuable tools in the investigation and classification of neurotropic viruses. The presence of specific antibody in serum may be demonstrated by its capacity to prevent the agglutination of human or chicken erythrocytes by various viruses. This is accomplished by the reaction of the antibody with the virus particle, destroying the virus's ability to combine with the surface of the erythrocyte. The hemagglutinating antibody is less specific than the complement fixing antibody. It, however, has been very useful in studying the immunologic relationship of the various neurotropic viruses.

### Neutralization

The neutralization test is the only test that measures specific antibody against the neurotropic viruses. Neutralizing antibodies usually appear in the circulation earlier than do other antibodies and often persist throughout life. The patient's serum is mixed with a known neurotropic virus. The antibody is then demonstrated by the inability of the virus to infect and kill the host, usually a white mouse, embryonated egg, or, more recently, cells in tissue culture. Because of its persistence, a high titer of neutralizing antibody is not indicative necessarily of a recent infection. It is necessary to demonstrate a rise in titer during the course of illness.

### Isolation

In addition to demonstrating a rise in antibody titer an attempt may be made to isolate the virus. Possible specimens suspected of containing virus are blood, throat washings, stools, cerebrospinal fluid, and brain obtained at surgery or post mortem. Cerebrospinal fluid and blood are not usually very satisfactory for routine diagnostic isolation but, in certain cases, may be of value. Stools are a very important source of polio virus and the primary source of diagnostic material in this disease. In those patients who succumb to their disease, brain material obtained at autopsy is the primary source of neurotropic virus. Viruses from these various materials may be isolated by suitably preparing the material and inoculating it into appropriate laboratory hosts. Mumps, lymphocytic choriomeningitis, and herpes may be isolated in the embryonated egg. Most of the other neurotropic viral agents may be isolated by intracerebral inoculation of adult or suckling white mice (except poliomyelitis virus, types

I and III) Characteristic phenomenon occur in those mice having virus present. The sick mice are sacrificed when moribund, and brain and other tissues are harvested and reinoculated into mice. This process is repeated until the virus is well established. The virus is then classified immunologically for final identification.

### Tissue Culture Technics

In recent years the employment of tissue culture technics for the isolation and study of neurotropic viruses has opened many new vistas and most virology laboratories employ this tool extensively. It has been especially valuable in investigating the enteroviruses, particularly the poliomyelitis and Echo (orphan) viruses. Poliomyelitis virus which has been studied most thoroughly to date produces characteristic cytopathogenic lesions in cells of the HeLa strain of epidermoid cancer cells. Tissue culture can be used also to demonstrate the presence of neutralizing antibody in serum. If neutralizing antibody is present in serum the capacity of the virus to destroy the cell is inhibited and cellular degeneration does not occur. Cellular degeneration may be seen microscopically or may be demonstrated by the absence of pH change in the media, an indication of the disruption of cellular metabolism. Because of rapidity of diagnosis, ease of handling and economy tissue culture promises to become a progressively more important tool for isolating and studying neurotropic viruses.

### SUMMARY

The virology laboratory has made available to the clinician technics for etiologic diagnoses of central nervous system virus disease. Generally the most useful tests are serologic because of their technical simplicity and because of their ability to demonstrate an antibody response in paired sera after about 10 days following the onset of illness. Usually primary isolation of the virus is more difficult and as a result, diagnosis less rapidly established. However the use of tissue culture has altered this in some respects. Tissue culture technics have greatly accelerated the diagnosis of certain neurotropic virus diseases and the future undoubtedly will see an increase in the speed of diagnosis as well as in the spectrum of agents capable of being identified. By consulting the virologist early in suspected cases of aseptic meningoencephalitis the physician and the patient as well as medical science will benefit.

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With few exceptions sickle-cell individuals are unable to concentrate urine normally although clinical tests of renal function yield no other evidence of impaired renal function.

Thus the defect which is exhibited by sickle-cell individuals is probably physiologic or metabolic in nature rather than anatomic. Its presence does not depend on the simultaneous occurrence of anemia but it is associated with the presence of sickle-cell hemoglobin. It appears therefore to be inherited as part of the over-all picture of the sickle-cell state.

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# RESPIRATORY STUDIES IN PATIENTS BEING CONSIDERED FOR COMPENSATION

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MILITARY patients offer an unusual opportunity in the study of personal motivation as it relates to compensation for disability. This is true because patients who are considered not capable of performing unlimited military duty anywhere in the world are presented to a Physical Evaluation Board for evaluation and disposition. The patient is usually given financial compensation when he is discharged from the service because of a disability. In general patients scheduled to meet a Physical Evaluation Board seem to have a greater tendency toward hypochondriasis and/or malingering than the other patients. This seems natural for the more disability a patient has the more money he gets in compensation. The relationship of this compensation factor to medical care is widely recognized. In a recent study of patients with acute low back sprain treated by conservative means Krusen and Ford found that only 55.8 per cent of 272 patients eligible for compensation were rated improved at the time of discharge. This compared with 88.5 per cent of 937 patients not receiving compensation. Furthermore the compensation cases required longer hospitalization and more frequent treatment than the other patients. There is an increasing need for information of this type as the number of compensation cases in the military in industry and in the courts of law grow more numerous every day.

The study reported here was devised to evaluate motivation and certain psychologic tendencies in military patients eligible for compensation. Initially the study was to consist of testing with the maximum breathing capacity. Inasmuch as this test depends on ability to breathe at sustained high velocity motivation to co operate and perform well is important for a high result. Subsequent thought and consultation led to combining a carefully devised questionnaire on respiratory symptoms with the maximum breathing capacity test. In addition the patients were given a modified Minnesota Multiphasic Personality Inquiry (MMPI) to evaluate hypochondriasis hysteria anxiety faking lying defensiveness and general attitude. Patients with dis

eases expected to produce respiratory symptoms or insufficiency and patients with psychiatric diagnoses were excluded. Thus, all patients would theoretically have no respiratory symptoms and a maximum breathing capacity in the normal range of the "predicted" maximum breathing capacity. Patients scheduled to return to duty served as the control group. This report deals with the methods, results, and conclusions of the study on the respiratory symptoms and the maximum breathing capacity revealed in the two groups. The results and conclusions of the other phase of this study are included in another report.<sup>2</sup>

### METHODS AND MATERIALS

One hundred servicemen from the wards of the U S Air Force Hospital, Maxwell Air Force Base, Ala., were studied between August and November 1957. Fifty patients (hereafter referred to as Group A) were scheduled to meet the Physical Evaluation Board, and 50 patients (hereafter called Group B) were scheduled to return to duty. The patients were selected, with the consent of the patient's physician, to answer a psychologic questionnaire and to take a maximum breathing capacity test. Each serviceman studied had no sign of chest disease by physical and roentgenographic examination which would be expected to produce respiratory symptoms or impaired ventilation.

The patients were called to a special room, where a noncommissioned officer monitored the questionnaire. Twelve questions were related to respiratory symptoms. The patients were not told the purpose of the test, and inquiries about the test received nonspecific answers. After the questionnaire was completed, the patients returned to their wards. In a few hours to a few days the patients were called to another room where another noncommissioned officer conducted the maximum breathing capacity test. In this way an attempt was made to keep the patients from associating the questionnaire with the ventilation test. The personnel conducting the tests did not know whether a given patient was in Group A or in Group B. This served to increase the objectivity of the test. All patients in the study co-operated fully.

A Collins 13.5 liter respirometer was used to test the maximum breathing capacity. Resistance to air flow was reduced by removing the soda lime container and the valves inside the spirometer. The test was performed with the patient in the standing position. Patients were told and shown how to breathe deep and fast into the respirometer. There was a short practice period before the test was performed for 12 seconds. After additional instruction, if indicated, and three minutes' rest, the test was repeated. The better test was recorded. The "predicted" maximum breathing capacity was calculated according to the formula devised by Motley<sup>3</sup>  $(97 \frac{\text{age}}{2}) \times M^2 BSA$



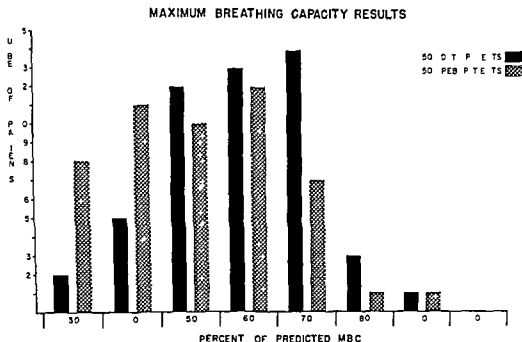
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Eighteen per cent in Group A have a maximum breathing capacity that is 70 per cent or above the predicted value, compared with 34 per cent in Group B. The groups are about equal in the 50 to 69 per cent range. It is noted that not a single patient in



*Figure 2 This graph shows a general tendency for patients in Group A to have a lower per cent of predicted maximum breathing capacity than patients in Group B. Each division represents a range of 10 percentile points e. g. 30 to 39 per cent, 40 to 49 per cent, et cetera.*

either group had 100 per cent of the predicted maximum breathing capacity. It is evident that the patients in Group B performed this test somewhat better than patients in Group A.

### DISCUSSION

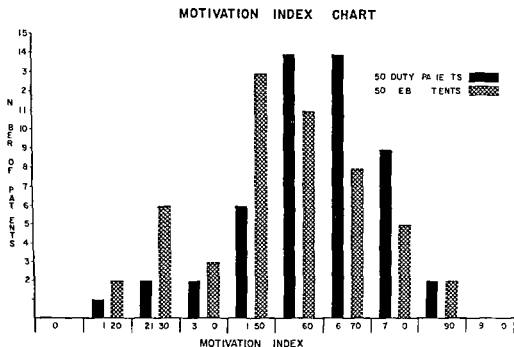
This study provides evidence to support the assumption that patients who may receive compensation for physical disability show more evidence of hypochondriasis than other patients. Neither the patients being considered for retirement from the Air Force for physical disability (Group A) nor the control patients returning to duty (Group B) were expected to have respiratory symptoms. Both groups were expected to have maximum breathing capacity tests in the normal range. Though patients in both groups had respiratory symptoms and showed values generally below the normal range of predicted maximum breathing capacity, patients in Group A complained more and performed more poorly on the ventilation test than patients in Group B. This trend is unequivocal.

The low values obtained on the maximum breathing capacity for both groups are probably due to two factors. First the patients represent an average group of young and middle age men who have maladies. The formula for the predicted maximum breathing capacity is based on results found in healthy students and other very healthy strongly motivated people. Even so different technics and calculations used in different laboratories will produce results that vary as much as 32 per cent and the standard deviation in a given laboratory may be 25 to 35 per cent. The formula recommended by Motley and used in this study has a standard deviation of 13 per cent. As far as we know a significant study on the "norm" for patients without chest disease has not been made. It is possible therefore that the formula used to determine the per cent predicted maximum breathing capacity in these two groups is not applicable in patients who have no apparent embarrassment of ventilation. Second the patients were not encouraged in a firm voice to breathe deep and fast deep and fast as the test was being performed. The technic of letting the patient determine the rate and depth of respiration after proper instruction and demonstration has been recommended.<sup>7</sup> This technic was followed in the present study. Subsequent testing on normal subjects in this laboratory has shown that constant urging and pleading with deep and fast deep and fast produces values about 25 per cent higher. However the extra effort exerted with the more vigorous technic would certainly be too much work for some patients. These two extremes in conducting the test indicate another problem in standardizing the maximum breathing capacity. Even though the factors mentioned above may account for the low maximum breathing capacity values the factors were constant in both groups. Therefore the relationship between the results in each group remains valid for the purpose of this study.

A logical sequence of this study would be to aid the physician in detecting the individual who has significant hypochondriacal or malingering qualities. This would be of value not only in the evaluation of compensation cases but also in predicting the patients who might respond poorly to elective operations. *Obviously patients with diseases of the chest could not be included.* A hypochondriac or malingerer in this study would be expected to have many respiratory symptoms and a low per cent predicted maximum breathing capacity. The patient who does not have these characteristics or one who is strongly motivated would be expected to have few or no respiratory symptoms and a high per cent predicted maximum breathing capacity. The term motivation index has been coined to express this quality in a patient. Using the respiratory symptom questionnaire and the per cent predicted maximum breathing capacity one could devise a formula to represent the motivation index as a numerical value. A simple formula would be per

cent predicted maximum breathing capacity minus the number of positive answers on the respiratory questionnaire Briefly stated, it is Motivation Index = % (P) MBC Respiratory Symptoms (S), or  $MI = \% (P) MBC \ S$

When this formula is applied to the findings of each patient in Group A and Group B, the distribution is as charted in figure 3 According to the assumptions made, the hypochondriac, malingerer, or poorly motivated patient would have a low score



*Figure 3 This graph shows that patients in Group A tend to have a low motivation index than patients in Group B*

A well motivated patient would have a high score Forty eight per cent of the patients in Group A have a score of 50 or less, compared to only 22 per cent of patients in Group B This ratio is reversed at the higher level Thus, patients in this study going to a Physical Evaluation Board are more than twice as likely to have a low "motivation index" as defined here as are patients returning to duty It is obvious that there is considerable overlapping in the groups

This type of calculation, using respiratory symptoms and a ventilation test to produce a numerical value defining motivation may be considered an invasion of the art of medicine Some may believe it is an attempt to substitute "mechanomedicine" for the observation at the bedside or the careful description of psychosomatic factors On the contrary this approach is an attempt to supplement the methods available which aid in defining certain intangible characteristics in patients

Several problems developed in the course of this study which were not anticipated in the original research plan. Six patients in Group A were eventually returned to duty without meeting a Physical Evaluation Board and eight patients in Group B were sent to the Physical Evaluation Board. At the time of the test, however, the patients were aware of their probable disposition as reflected in this study. Nevertheless, future study must be done when the disposition is certain. Secondly, some of the answers referring to the respiratory symptoms may have been affected by a medical problem that was unrelated to the lungs. However, it is very difficult to devise questions that would refer only to the lungs and chest. Thirdly, a more positive correlation might be expected if the patients were aware of the purpose of testing and if the time interval between the two tests were short. These problems must be considered in the plans for future investigation.

### CONCLUSIONS

The deficiencies of this testing procedure include all the problems that are acknowledged to make psychologic questioning and pulmonary ventilation tests of limited value. However, the use of an adequate number of control patients will nullify these objections in a study of this type. The formula which offers the motivation index is not clinically applicable now. More patients must be studied and adjustments must be made in the testing technique. Further investigation along this approach does seem warranted for assumptions on the symptoms and behavior of patients considered for compensation have been supported.

### SUMMARY

One hundred military patients have been studied to evaluate motivation and the tendency to hypochondriasis in compensation cases. A combination test was employed which consisted of a questionnaire on respiratory symptoms and the maximum breathing capacity. All patients had normal chests and no significant emotional illness. Fifty patients were scheduled to appear before the Physical Evaluation Board and 50 patients were scheduled to be returned to duty.

In general, the patients returning to duty had fewer respiratory symptoms and higher results in the maximum breathing capacity than the patients who were potential compensation cases. There were exceptions to this trend in both groups.

A reliable test of motivation or tendency to hypochondriasis would be of value to physicians who are concerned with compensation cases. Such a test would also be helpful to a surgeon evaluating a candidate for an elective procedure. Interesting speculation is presented on a method to determine the motivation index using information gained in this study. The

limitations of this information and the need for further investigation are discussed

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## BENEFICIENT STRESS\* IN RETIREMENT

Even though we may have retired from our jobs each of us needs something to do that is purposeful and constructive. We live in a society that emphasizes that man's role is a creative and constructive one. Most of us have worked steadily and industriously in a society that respects only the productive. We have become accustomed to a certain amount of stress. This is the vital elixir of life. Regardless of age it is essential in the proper dosage to the maintenance of health and happiness. The stress that has stimulated us in our lifework must be replaced in retirement by the use of the "beneficient stress" that comes from new pursuits—vocational, avocational, educational, cultural, and recreational. There is an adage: action absorbs anxiety. Applied to the individual who is preparing to retire, purposeful activity under the ceiling of stress not only absorbs anxiety but also prevents both physical and emotional deterioration.

—HOWARD A. RUSK, M.D.  
EUGENE J. TAYLOR, M.A.  
in *Journal of Chronic Diseases*  
p 446 May 1958

# THE HOWARD BAILEY TOURNIQUET

STERLING J RITCHIEY C I I MC USA

**T**HE Howard Bailey pneumatic tourniquet has proved so successful at this installation that dissemination of information concerning this unique but simple device seems justified

Dr Lot Howard of San Francisco Calif demonstrated this tourniquet at the Gadget Exhibit during the meeting of the American Academy of Orthopaedic Surgery in 1956 Its simplicity reliability and economy prompted its construction and testing here With minor variations from the original this tourniquet has been used in the operating rooms at this hospital exclusively for over one year with amazing freedom from technical application errors and mechanical failures

## DESCRIPTION

The arm tourniquet consists of a blood pressure cuff or other pneumatic arm cuff enclosed in its removable cloth sheath or sewed into a strong cloth cover The cuff cover is sewn at its edges to a strip of flexible metal fireplace screen which is the size of the cuff itself The arm cuff (fig 1) measures 23 by  $3\frac{1}{2}$  inches and this size seems ideal for adult arms and as a leg tourniquet for small children The leg cuff measures 31 by  $3\frac{1}{2}$  inches is constructed in the same manner and utilizes a commercial leg tourniquet rubber bladder The hook is formed of spring steel wire 0 105 inch in diameter

Another a child's size 16 by  $3\frac{1}{2}$  inches is occasionally used Any two tourniquets can be hooked together for the very large extremity The tube outlets of the tourniquet bladder are cut off and cold patched with automobile tube patches A replacement valve stem is cold patched to the center of the bladder as a loading and deflation valve

The tourniquet simply is applied in one step with the firm application of the cuff about the extremity and the free hooks catching in any coil (fig 2) No additional bandage support is required The tourniquet is inflated in the same manner as an automobile tire with the application of the loading nipple at a predetermined pressure The loading tip the replacement valve

stems, and the cold patching sets are available at a nominal cost at any filling station or automotive supply store

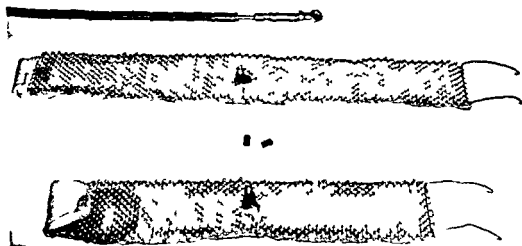


Figure 1 Two sizes of cuff with valve stems and the loading tip



Figure 2 Tourniquet in place and method of applying

A simple movable upright is fashioned from a 95 gallon tank of compressed gas or air with a regular welder's gauge. This tank connects beyond its ordinary welder's gauge. The gauge is an adjustable valve, the first dial gauge recording tank pressure (when the tank valve is open) and the second regular tourniquet pressure gauge. This shows the adjusted pressure in the delivery line of the tourniquet when inflated. The ordinary tourniquet



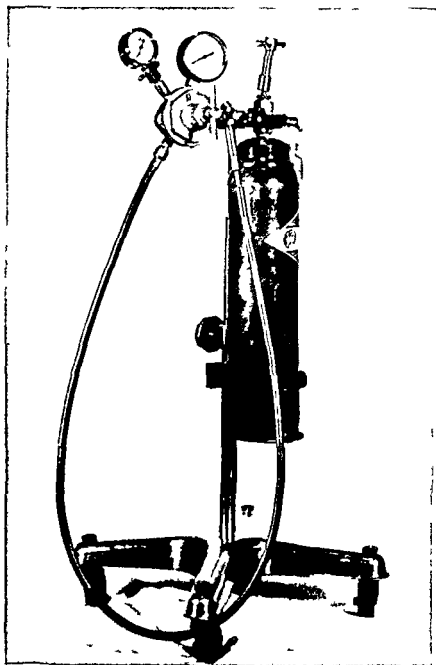


Figure 3 Gas tank and stand. Tank pressure gauge, liquid pressure gauge, reduction valve and load gauge

illustrated, is calibrated in millimeters of mercury, the type familiar to surgeons. If pounds per square inch (p s i) valves are used, which then would eliminate replacement of the second pressure gage, a simple conversion formula may be used:  $p s i \times 50$  equal mm Hg. Thus 6 p s i equal 300 mm Hg for arm pressure, 12 p s i equal 600 mm Hg for leg pressure. The tourniquet pressure desired is adjusted before the tourniquet is inflated. One quick loading application is required, and the stem cap is then replaced.

The tourniquet loading tank is portable. One tank is adequate in an operating suite of many rooms, and in a medical facility of this size, two cuffs of each size have proved to be adequate.

Extended tubing from the cuff is not recommended, inasmuch as these tubes are the usual source of leakage. Ordinary oxygen "D" tanks carrying 1700 p s i pressure are used, because they are more economical than compressed air tanks. There is no explosion hazard from the use of oxygen in this manner.

The tourniquet is extremely comfortable because of its broad steel mesh support, and it is much more simple to apply than are other types. In over one year of continuous use at this hospital, it has proved to be economical as well as completely reliable and trouble free.

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### PUSH BUTTON SATELLITES

In 1946 an American physicist Louis Ridenour published in *Fortune* a whimsical but prophetic piece. He saw the earth surrounded by a swarm of atom bomb carrying satellites owned by various nations. By pressing the proper button one of these deadly moons could be made to drop on a target anywhere in the world. In well protected underground operation centers the military of every nation were keeping day and night watch with their eyes glued to radar screens and their fingers on the fateful switches. An earthquake in California a misinterpretation of the blip it produced on the radar screen a snap decision of an overwrought officer—and the rain of atomic satellites began to fall upon the cities of the world as one nation after another was drawn into the deadly chain of massive retaliation.

—EUGENE RABINOWITCH  
in *Bulletin of the Atomic Scientists*  
p 350 Dec 1957

## SERVICE ARTICLE

# INDIVIDUALIZED RELIEF SERVICES FOR THE CIVIL WAR SOLDIER AND CURRENT SOCIAL WORK PRACTICE

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IT is easy to become diverted and to fall victim to the tendency to exploit the dramatic and spectacular when studying any aspect of the Civil War period. That it was a fascinating, colorful period of history is readily apparent in the incredible amount of historical material available to the researcher; for example, the entire bookstores which deal only with books on Lincoln and Douglas Southall Freeman's monumental *Lee's Lieutenants* with its staggering documentation.

This article spotlights a single phase of the Civil War period—a small part of a larger movement which in turn was a part of still larger movements. This particular phase of the Civil War period comprises the charitable activities related to the social and economic problems of sick and wounded soldiers and their relatives. Specifically, the article is centered about the hospital visitor program sponsored by the Special Relief Department of the United States Sanitary Commission during the period 1861 to 1865 and its relationship to modern military clinical social work as the earliest recognizable expression of an activity identified today as social casework.

Because the flowery language characteristic of the Civil War period requires special attention to semantics, quotations are employed to a far greater extent than would ordinarily be desirable so that the reader can determine for himself whether the material has been interpreted fairly and accurately. Extensive quotation is also indicated because of the nature of the study. The comparison of an activity unique to the American Civil War with an activity identified today as social casework involves a judgment concerning professional goals, philosophy, concepts, principles, and methodology. Inasmuch as none of these is entirely objective, the reader can use the numerous quotations to verify for himself the conclusions reached in this article.

## INTRODUCTION

The fall of Fort Sumter in April of 1861 gave birth in the North to a burst of human activity that can hardly be imagined. Within three days over \$1 000,000 was spent on flags. More would have been spent, but the supply was exhausted. Every available piece of red, white, or blue bunting was snipped up almost overnight and made into dresses, bows, or other ornamentation. States that were asked to provide one regiment responded with ten. Men, jammed into cattle cars, stood without food or water for 36 hours in a frenzied rush to the defense of Washington. An avalanche of bandages, lint, clothing, and food crowded every rail center in the North. Ladies Aid Societies were organized overnight. Bands played, bells rang, and bars never closed in that first burst of patriotic fervor.

Lincoln had asked for 75 000 volunteers, and in less than two weeks 350,000 were organized into crude, motley, unarmed bands of fevered men. The National Government was ill prepared for anything like the organization and direction necessary for this scale of activity.

The Regular Army numbered only 17 000. They were scattered out on the frontiers as far away as California. How were they to organize, train, and lead a volunteer army that outnumbered them more than 20 to 1? This was no orderly, regulated induction. One day they numbered 17 000—two weeks later, 365 000.

Medical care for the peacetime Army was organized into a Medical Bureau totally unprepared for mobilization. Preventive medicine was almost unknown to the Army, which also lacked facilities, a hospital system, and even a semblance of an evacuation plan. In brief, they were set for garrison medicine, not for field medicine.

And now thousands of inadequately equipped, undisciplined, but enthusiastic, volunteers came tumbling into makeshift camps having almost no sanitary provisions. The fatigue, the malnourishment, the unaccustomed exposure to the elements, the indiscriminate billeting of persons from all points of the union, the flies, and the latrines combined to lay half of the troops low with fever, diarrhea, dysentery, and malaise.

The "home folks" were not long kept ignorant of the fact that "their boys" were in a bad way and that their government was inadequate to handle the situation with the dispatch necessary. Letters home intensified the activities of fathers, mothers, sisters, and sweethearts to a level of motor activity that can only be appreciated by the results obtained. A noted historian of the period, Emerson David Cite,<sup>2</sup> was of the opinion that never before in the history of the United States had such great charity existed.

From strait-laced tranquillity and unbending propriety young ladies became strenuous volunteers

Everywhere the sewing machines were driven at their utmost speed and paused not even for the rest of the Sabbath in preparing needful articles of clothing and needle women scarcely less swift in their labors of love worked till the gray dawn streaked the East and after the briefest possible interval of rest returned anew to their toil While everywhere fair brows grew grave with thought of what could be done for those who were going forth to fight the nation's battles<sup>1</sup>

Even the divines were stirred A Parson Brownlow declared We are ready to fight for this flag till Hell freezes over and then we'll fight on the ice

This then was the vitile strenuous response of a people a people marked by self-righteous morality distinguishable by their worship of God work and cleanliness captivated by the love of hyperbole enamored of the sententious and flowery phrase preoccupied with thoughts of death, and given to black suits black hats black dresses and black shoes Hark from the tombs a doleful sound conveys as well as a phrase can the temper of the time just prior to the outbreak of war

#### THE UNITED STATES SANITARY COMMISSION

There are few more inspiring stories in our history than that of the growth and development of the United States Sanitary Commission After reading the account of its origin and subsequent success one is struck by the fact that it is so little known

It was no indiscriminate holiday scramble of Good Samaritanism It grew out of what was initially an irrepressible wave of national ardor good will and self-sacrifice at first motivated by the call to arms but later by the accounts of the frightful suffering of the troops in camps even before a shot was fired

The first charitable efforts of the Nation were guided by nothing more than common sense If the troops were starving send food And send food they did Mountains of it stacked up at railroad terminals and rotted in the summer sun If they were in need of clothes then send clothes And all kinds of garments clogged the overtaxed supply lines If medicines were needed send medicines If tender loving care was needed then go and join the troops

All of these things happened before the government could stem the tide of charity which was literally inundating the Washington area

When word of the chaos resulting from the spirited and well-intended efforts of the people got back to them they promptly

introduced sound method and system to their work Ladies' Aid Societies carefully planned ways for determining need, distributing work, raising funds, corresponding with the National authorities, and bringing general order and co ordination to the home forces

Among the first Ladies' Aid Societies was the Women's Central Association of Relief of New York City Organized in April 1861, it assumed leadership in impressing upon the Federal Government the need for a more effective program for the care of sick soldiers They carried on an extensive correspondence with other societies, urging them to pummel the government with letters demanding action In its membership were ladies from the leading families of New York City, who succeeded in getting a number of doctors, ministers, and other influential laymen to petition the President On 18 May 1861, a petition reached President Lincoln asking him to organize or encourage the organization of a commission, composed of civilian and military leaders, to be "charged with the duty of methodizing and reducing to practical service the already active but undirected benevolence of the people for the comfort, security and health of the Army "

The President and the Secretary of War did not at first look with favor on the proposed plan which they regarded as a sentimental scheme concocted by women, clergymen and humane physicians " Only the earnestness of its advocates, their high position, and the support of the Acting Surgeon General of the Army dissuaded them

Accordingly, on 9 June 1861, the President approved a commission called The Commission of Inquiry and Advice in Respect of the Sanitary Interests of the United States Forces and later changed to The United States Sanitary Commission ( USSC)

It was composed of some 500 doctors, clergymen, professors, Army officers, and other interested citizens Its mission was seen as largely medical and nursing, but they had as an additional objective whatever else relates to the care, relief, or cure of the sick and wounded "

The USSC was a civilian commission with Presidential approval to inspect Army facilities and make recommendations It had no executive functions within the Government structure As to relief of the sick and wounded, it was intended to support, not supplant the Army Medical Bureau (later changed to Medical Department)

It is not necessary to go into the functions of the USSC except to make clear its broad purposes and pattern of functioning At the request of the Army, it met service and material needs as they became apparent and it co ordinated the philanthropic efforts of the nation

## SPECIAL RELIEF DEPARTMENT OF THE USSC

In the early reports of USSC activities there is no mention of what today would be referred to as social casework. The very detailed "Camp Inspection Return Form" which covered everything from bedbugs to drunkenness makes no reference to individualized charitable activities. Inspection returns during July 1861 on the hospitals around Washington D C make no mention or recommendations which can be interpreted as coming within the broad area of what we now consider medical social work.

In time however special or individual needs became evident. Mr. Fredrick N. Knapp was designated Special Relief Agent. In his first report 23 September 1861 he spoke of providing aid and comfort to sick soldiers passing through Washington. This help was individualized and given with sympathy, understanding and good cheer.

J. S. Newberry, head of the USSC in the Western Department, gave this explanation for the establishment of a Special Relief Department:

early in the history of the war many unexpected things as we first supposed. The exceptionless claim of our sympathy and effort while suffering from one or another of the thousand hardships or misfortunes which are the legitimate fruit of every system controlled by finite and imperfect men.

Thus there grew up under the leadership of Mr. Knapp (a clergyman) a program of service for sick soldiers who were in transit from one hospital to another or on their way out of the service as a result of wounds or illness. These services included transportation arrangements, aid in correcting soldiers' papers, getting back pay, recovering them their positions when they have been wrongly set down as deserters and saving them from sharpshooters, and as the war progressed aid in procuring pensions and bounties. All of this was aimed toward the relief of that most terrible mental anguish, the torture of dread uncertainty.

The Special Relief Department also looked toward rendering the sick soldier content by providing care for his family. This was achieved through material assistance, advice, health and welfare reports, and through the establishment of a directory service listing sick and wounded soldiers and their location.

Typically Special Relief Department services were rendered from Soldiers' Homes which were in actuality facilities for transient soldiers. These services were not rendered in relation to medical conditions. They were meeting social needs of sick and injured soldiers but not in a medical setting. Any medical care needed was secondary. It cannot be considered as entirely analogous to present day medical social casework. But the

important thing to recognize here is that need was recognized and met on an individual basis

The Special Relief Department agents exhibited a concern for the individual and a philosophy of help that comes close to the underlying social policy of today which manifests itself as social casework. Special Relief Agent Fredrick N Knapp's third report, 21 March 1862, says of their mission of providing "aid and comfort "

It is something more than bestowing food and clothing or alleviating pain it is relieving a mental anxiety what a vast amount there is in the hearts of these soldiers of personal sacrifice daily struggle to put down anxious feeling which might enervate the man the sum and costliness of all this can never be estimated \*

This was not merely a conviction or a belief, it was transformed into a program of services. Mr Knapp, in the report cited above said of one of these early workers, a Mr Rogers "His judicious advice or timely direction or helping hand has saved men from anxiety or real suffering " These individualized services are described as taking from 30 minutes to a half day "and the aggregate of all the pain saved has been greater than any person not cognizant of the variety and the number of these calls could estimate "

Others, like Mr Rogers, who worked in the soldiers' homes, found that "to unite tender kindness and cordial welcome with the exercise of a discriminating judgment, and often stern authority is not easy, in our Special Relief work the presence of the one does not exclude the working of the other, and that not the soldier only, but the Army is stronger because of the home "

A number of typical case recordings of these soldiers' home "caseworkers" appear in Report No 77 of the USSC. These recordings probably among the first, read like a typical record from a present day relief agency. The "caseworker" of that day was required to have a knowledge of community resources. That he made referrals is revealed by this comment appearing in the same report "This work has consisted in judiciously as signing the applicant for aid to such existing Relief Associations in the city as his case pointed to "

The Special Relief Department marked the first step within the USSC to provide individualized social service for the incapacitated of the Union Army. But as the Army increased its capability for handling sick and wounded, opportunities began to present themselves to reach sick and wounded soldiers in the hospital, where they were one echelon closer to the battlefield.

A partial understanding of the principles underlying the practice of the Special Relief agents can be gained by a review of



The report cited above goes on to give a number of instances in which indiscreet actions of overzealous friendly visitors militated against recovery of the patient

Mr Newberry in his book offers this advice to hospital visitors on developing a relationship

He (hospital visitor) should know how to approach men with judgment and discretion so as not to repel but to draw them not to shut up their hearts but to open them not to kill but in every sense to cure

This is more than a mere blind groping toward what modern casework refers to as building a relationship

There are recurrent references to the need for trained disciplined personnel to provide these services It was not seen as a momentary orgy of self sacrifice although in many instances the services of these persons could be so described They often worked without pay They exposed themselves to the ravages of disease The stench from the hospitals is described as just short of unbearable The hours were long and the elements often severe Many died as a result of overwork Nevertheless the commission insisted and the wisdom of the stand was not questioned He or she must come as distinctly under an obligation of duty in this respect as if under pay and must submit to the same discipline

Dr J W Bellows President of the USSC had this to say of the hospital visitors

Only a few who had a genius for the work continued in it and succeeded in elbowing room for themselves through the never ending obstacles jealousies and chagrins that beset the service Every woman who keeps her place in a general hospital or corps hospital has to prove her title to be trusted her tact discretion endurance and strength of nerve and fibre they carried into their work their womanly tenderness their copious sympathies their grateful devoted devotion and had to face and contend with the cold routine the semi-savage professional indifference which makes ordinary medical supervision in time of actual war impersonal official unsympathetic and abrupt Their position was always critical equivocal suspected and to be justified only by their undeniable and conspicuous merits justified by the love and reverence they exacted from the soldiers themselves

Among those who survived or measured up was Miss Helen Gilson She is described as delicate beautiful and possessed of an inimitable manner Her doctrine "The less a creature has had in the past the more he ought to have now" Another was Miss Mary Safford who was among the first hospital visitors

She also introduced occupational therapy into military hospitals during the Civil War

Mary A Livermore is one of the strongest charitable figures of the day While mostly known for her success in fund raising through "Sanitary Fairs " she nevertheless took a whirl at hospital visiting Speaking of sick, but ambulatory patients, coming to her office for material assistance, she said

They tarry to talk over their trials sufferings and privations and their anxiety to get well and join their regiment They are praised heartily petted in motherly fashion as if they were children which most sick men become urged to come again and sent back altogether lighter hearted than when they came "6

She passes on to us also one of the few recorded vignettes of "casework" to come out of the war

Doctor to Hospital Visitor (Mary A Livermore) All you can do is to help him to die easy

Patient What does the doctor say? Oh I know I must die I can t' I can t' I can t'!

Hospital Visitor Why are you afraid to die? Tell me my poor boy

Patient I ain t fit to die I have lived an awful life and I am afraid to die I shall go to hell

Hospital Visitor (*putting hands on his shoulders and speaking in commanding tones as to an excited child*) Stop screaming Be quiet This excitement is shortening your life If you *must* die die like a man and not like a coward Be still and listen to me

The Hospital Visitor then proceeds to combat the patient's fear of death and his sense of guilt with assurance of God's willingness to pardon "6

There are numerous instances of hospital visitors helping soldiers to die This was, however, more often a chaplain's job when the end approached

The hospital visitor, contrary to the title, was not a fly by night More often he or she was a regular staff member in the sense that he or she was there regularly Among their many functions were arranging for furloughs or sick leaves, straightening out pay matters, consoling relatives, providing amusement, writing letters, listening to the patients' woes, arranging for transportation, correcting false charges of desertion, and providing small incidental articles and delicacies While hardly up to today's standards of medical social work practice, they seem to be a relatively close fit, at least with reference to functions and goals

## OTHER WORK WITH THE SICK AND WOUNDED

## Refreshment Saloons

One of the facilities that grew up in response to a need during the first flush of mobilization excitement and remained to become an institution for the duration of the war was the Refreshment Saloon. Originally set up as temporary shelters for volunteers on their way to Washington in response to Lincoln's first call they were intended as overnight quarters—a place to clean up and get a bite of food—but like other facilities and efforts, they quickly adapted to changing needs and more extensive demands. The refreshment saloons were also an ideal outlet for the charitable urges of the people.

One of the most famous of these saloons was the Cooper Shop Volunteer Refreshment Saloon in Philadelphia. Commended as an emergency measure, it became a permanent oasis for transient soldiers and relatives. It expanded to include hospital facilities. It is this feature of its work—as well as its work with relatives seeking a son or husband who had become a casualty—that makes these saloons important to our story. For here, too, there is an evident pattern of meeting human needs which takes on a character highly suggestive of modern day social casework services.

One should not let the language of the following extract obscure the manner in which these services were provided. Such comments should be more appropriately interpreted as the spirit in which the services were given.

To the returned soldier it is their first home—a home like they knew in y<sup>er</sup> with their little world in which comforts abound and smiling faces shine. It may be called an oasis on life's path—a y<sup>er</sup>—a green spot in an icy world.<sup>17</sup>

When a soldier's emaciated form and sunburned face appeared at the Cooper Shop, he was given a hearty welcome, taken to a lavatory and thoroughly cleansed and presented with a change of clothing. Then

The feelings of the individual were entered into and while partaking of a cup of coffee they were drawn out whether he came from the granite hills of New England, the fair fields of the fertile Ohio, or grass-clad plains and smiling sacred valleys of our own Pennsylvania. Warming under this genial influence, he would tell of the loved ones he left at home or the hairbreadth escapes he met by flood and field or in the imminent deadly breach. Then would the tears flow down the cheeks of the hardy soldier. His pay he would send to his wife at home and the children, the objects of his care and love. Was a letter to be written? Then the Lady Principal had this attended to. (speaking of one of these lady principals—Miss Anne M. Ross) She entered into the little

confidences that are so potent in their tendency to do good, and nothing in which the well being of the patients were concerned escaped her quick eye <sup>17</sup>

What kind of a person was she the refreshment saloon "case worker?"

She had a frank free open and sincere manner that spoke to the understanding and heart a power of persuasion very rare an eloquence that is less easy to describe than conceive consisting in the well directed application of the thoughts that spring up in a ready mind <sup>17</sup>

If the language of today could be substituted for the language of that day, there is much in the above which is directly applicable to present-day casework—sensitivity to need starting where the patient is, nonjudgmental attitudes, individualization, respect for the human spirit

#### U S Christian Commission

Many members of the Union clergy were heavily involved with the USSC however, the group was also organized into the United States Christian Commission (USCC) "to minister to the spiritual wants of sick and wounded "

Their early efforts included evacuation of the wounded from the battlefield, providing food, administering to the dying, and spreading the Message of the Gospel

This last was probably the first motivation or stimulus as reflected in such statements as these

The soldier has a soul as well as a body a soul to be blighted and polluted by the vices of the camp or to be kept pure and holy for that change of worlds which to so many must come with fearful suddenness They would invoke healing mercies for both soul and body from the Great Physician and point them in the struggle with the last enemy to Him who is Abolisher of Death and Conqueror of the Grace <sup>3</sup>

To judge by the eyewitness accounts of deaths occurring in hospitals, these chaplains were wondrously effective By their gentle ministrations, firm admonishments to ask God for forgiveness, supplicatory prayers, and soothing hymns sung "in full rich baritone filling the entire ward," the dying soldier was transformed as if by a miracle from a frightened, desperate, tormented soul to one who faces death with calm peace and a "look of inexplicable radiance and beauty as he passes into the Last Land The reader must make his own evaluation of these accounts but one thing is unmistakable—the accounts of such beneficent effects are overwhelmingly abundant These accounts are not limited to those of the clergy but include those of soldiers, nurses, hospital visitors, and military leaders

As the struggle wore on, the clergy turned increasingly concerned for temporal wants without, of course neglecting spiritual. Grace Marcus was anticipated by more than a century:

Understanding fully that there is sometimes more Gospel loaf of bread than in a sermon it bestows the loaf of bread it is needed and the Gospel also.<sup>3</sup>

They stood firm on the need for both the spiritual and temporal aspects of giving. The two could not be effectively separated.

These money gifts are all good and indispensable to the accomplishment of the great purposes desired but by the side of the spirit of self sacrifice the gift of personal service the dedication of an earnest and generous nature to the work how precious and worthless do they seem.<sup>4</sup>

Tradition dies hard, but a marked shift in emphasis is indicated in Mr. Frederick Knapp's (himself an eminent clergyman) Third Report of the Special Relief Department, 21 May 1918 when he said:

A miserably poor thing are priestly robes and Sunday sermons unless joined to a spirit and a hand which take hold of the work of helping men who need assistance.<sup>5</sup>

It is of interest to note how quickly these volunteers adapted to the needs without sacrificing their original purpose.

#### The Army's Program

As indicated earlier the Army was unprepared at the beginning of the war for the sudden mushrooming of medical needs. As the war progressed they developed facilities, programs, and personnel to take over areas of responsibility which had been met earlier by the USSC. Yet it is interesting to note that in the U. S. Army Medical Department's official *Manual of Hospital Stewards*<sup>11</sup> (very comparable to our present-day lay administrator's manual) which carefully outlined the duties of hospital personnel as well as hospital functions there is no mention of hospital visitors or of any functions which were carried out by hospital visitors. This is even more surprising when the manual of its publication (1863) is taken into consideration.

Now it can hardly be asserted that responsible officers were unaware of this need, because frequent references can be found of medical officers praising the persons performing these functions and emphasizing the need for such services.

Nurses were as new to Army medicine as hospital stewards but their duties are outlined as are those of attendants. Of course there is a difference here they were employed for a salary (12 dollars a month and all they could eat) and

employees were more closely identified with the structure yet, even when this is considered the question remains "Why weren't the hospital visitors employed as paid personnel?"

The tradition thus established remained until 1 July 1951, when the Army recognized medical social work as an essential part of comprehensive medical care, and uniformed personnel took over responsibility for this function from the American Red Cross

### Individually Inspired Efforts

The U S Sanitary Commission, the U S Christian Commission, and the refreshment saloons were organized, stable, charitable programs. In addition, there were a number of less organized sporadic benevolent efforts. These were largely individually inspired exploits. Many were lone operators ranging around the battlefields, meeting the needs of wounded and dying soldiers. Some women served as soldiers and fought with regiments. A few like Mrs. Turchin, wife of Colonel Turchin, even took over leadership and fought with the regiment in battle. Still others just set out "to relieve right then and there such needs as were most pressing, making themselves useful in any way they could among the sick and the wounded."<sup>15</sup> General Slocum was so taken with one of these, Miss Amy Bradley, a school teacher from Kennebec County, Maine, that he ordered "henceforth you are in charge of everybody in this brigade who is sick or in trouble."<sup>16</sup> Miss Bradley may well have been the first military social worker to be recognized by a responsible commander.

## DISCUSSION AND CONCLUSION

### A Comparison of Early Casework With Special Relief Activities

If it is to be accepted that Mary Richmond represents at least one of the first persons to define social casework, it may be of advantage to compare her thinking with the practice of agents of the Special Relief Department of the USSC. This is her well known definition: "Social casework consists of those processes which develop personality through adjustments, consciously effected, individual by individual, between men and their social environment."<sup>17</sup> By this definition, as elaborated in her book, *What is Social Casework?*, she definitely had in mind personality change, personality improvement, and improved adjustment in human relations. It is doubtful that the Special Relief agents, whether hospital visitors or soldiers' home workers, had much more in mind than relief of immediate suffering or correction of a social disability. Their efforts appear to be more clearly aimed at tangible services. The special emphasis on social relations in Mary Richmond's book is not evident in the work of the Special Relief agents. They did, however, treat patients

individual by individual and did aim toward a better adjustment of the individual and his environment

Mary Richmond also spoke of social insights strengthening medical diagnosis. It is possible to read into some of the accounts of hospital visitor activities a recognition of this but a disciplined conscious employment of this insight by the doctor must be said to be absent from the practice of that day. She also speaks of social actions (tangible service) by the medical social worker as strengthening rehabilitation of patients. These actions she refers to range from the humblest services guided by affection, patience and personal sympathy to such radical measures as complete change of environment, the organization of resources when none existed before and the reknitting of ties long broken.<sup>4</sup> There is a strong resemblance here to the work of Special Relief agents.

How is the personality growth that Mary Richmond spoke of achieved? By an instinctive reverence for personality and a warm human interest in people as people.<sup>5</sup> The attitude of Special Relief agents could hardly be described better.

#### Comparison of Early Medical Social Work With the Hospital Visitor Program

Ida Cannon attributed the beginning of the civilian medical social service movement to Dr. Elizabeth Blackwell, the first woman doctor in America, who as early as 1853 saw the need of tying hospital and home together. (She makes only a passing reference to the USSC.) She defines this movement as follows:

What we call the Medical Social Service Movement had as its purpose to bridge the gap between hospital and community, to recognize their interdependence and to determine the relation of cause and effect in the patient's disease and his environment. At first this purpose was necessarily expressed in rather simple practical action directed toward the immediate need of the individual patient.

Without going into a detailed analysis, it is apparent that this statement describes well the hospital visitor program. The hospital visitor did bridge the gap through use of therapeutic follow-ups, health and welfare reports, material assistance, and recognition of the deleterious effects that concern for one's family would have on the sick soldier. Surely it would not be argued that our present caseworker isn't more skilled, but the important point is that these early Civil War workers recognized the problem and offered thoughtful, sensitive, practical, individualized assistance.

## Comparison of Civil War Relief Services With Current Social Work Practice

A direct comparison of present-day standards, basic principles, elements, concepts, and goals with those which emerge from an examination of the literature of the philanthropic efforts during the Civil War should be helpful in determining whether such efforts during the Civil War period could be considered the beginning of modern military social work

Harriett Bartlett, listed principles which define the relation of medical social work to the medical setting. Each of these will be taken individually, and compared with the practice of the hospital visitor

*"Social work should bring a unique contribution to the medical setting additional to and not duplicating the services already available"*<sup>21</sup> This was a basic operating principle of the entire USSC. The hospital visitor implemented it. There were no provisions for therapeutic furloughs, communicating with families, visiting relatives, helping sick and dying soldiers with social and emotional problems relating to illness, correcting pay matters, correcting improper charges of desertion, or for returning to civilian life. The hospital visitor provided for these needs.

*"Its objective should be in agreement with those of the medical agency and thus will focus upon social problems in illness and social problems in health"*<sup>21</sup> Report No. 50 of the USSC<sup>21</sup> discusses this in relation to working in responsible relationship to medicine. "The principle underlying the whole design of the commission is to work as far as possible with the approbation of the Medical Officers, furnishing supplies under their orders, or directly to individual cases after carefully examining into the real character of such," said Dr. Steiner, Chief Inspector of Relief, USSC.<sup>21</sup>

*"Social work should be organized as an integral part of the medical agency"*<sup>21</sup> This has been discussed. It was not an integral part of the Army or the hospital, but the same hospital visitors worked regularly in the same hospital, it was not sporadic.

*"Its most characteristic role will be to assist patients to benefit from and make effective use of the agency's services"*<sup>21</sup> This has been amply discussed. Actually, they went beyond this and created resources for unmet needs.

*"Since the work is always carried on in association with other professions teamwork is a basic method"*<sup>21</sup> There are, as has been pointed out, references to working with physicians, but no references can be found to working with nurses, for example.

*"Effort should be directed toward assisting members of associated professions in the getting to understand and deal more*



*effectively with the psychological needs of patients namely to enlarge their responsibilities and capacities in this direction* <sup>1</sup> Efforts of this nature were made particularly in the matter of granting therapeutic furloughs. One incident is cited of a hospital visitor carrying the issue up to General Grant who after conferring with his medical director granted the furlough. The *U S Sanitary Commission Bulletin* Number 18 describes an instance of a hospital visitor pointing out to a doctor the psychological value of a furlough for a patient.

With reference to the basic elements of social work Harriett Bartlett listed these <sup>21</sup>

*"Knowledge of human behavior (individual and group) and of social institutions"* Quite naturally the content of our knowledge is different from that of the Civil War period even as that of tomorrow will be different from ours. Yet, throughout that period we find references to such things as regression, dependency, malingering et cetera. They understood the importance of family and the soldier's home community. There are references to guilt, fear, and anxiety. In the discussion of the provisions for the disabled there are indications of their appreciation for and their knowledge of human behavior.

*A democratic philosophy, an attitude of deep respect for the personality, dignity and right of self-determination of the individual* <sup>22</sup> In this respect let us consider the philosophy of the Special Relief agents with regard to the disabled, their treatment of deserters, and the general philosophy underlying the Special Relief Department.

*"Skill in human relationship and in helping people toward better social functioning through use of their own strength and society's resources"* <sup>23</sup> The skill they had was apparently not a conscious skill. It appears to have been in the nature of an intuitive ability. Although it will be recalled that they emphasized the relationship, it cannot be inferred that it was used consciously as a tool in the way we consider the use of relationship today. But they unquestionably did employ the individual's own strength and society's resources in treatment as has been shown in the references to the hospital visitors' services.

*"An orderly scientific way of thinking about social factors and social problems"* In this it is difficult to make a comparison. Judged from a practical view they were orderly in their recognition and solution of social problems. Starting with chaos and no precedent they brought organization, program, and efficiency in an unbelievably short time. They were systematic and methodical. They operated in accordance with policy and procedures. It was not trial and error.

*"Awareness of one's own feelings and biases"*<sup>21</sup> From the material, one is obliged to conclude that this is an area which falls short of modern professional practice. There is no dearth of personal testimonials of their reaction to the problems of the sick and wounded soldier, but one cannot conclude from this that there was a conscious awareness of how this influenced their work with individuals. They had firm conviction as to what was right, often anchored in a religious philosophy. An understanding of transference and countertransference phenomena was not apparent. They did avoid hiring, and discouraged as relief agents, persons who approached their work as "a holy mission."

*"Disciplined performance in rendering social services to individuals, groups, and communities"*<sup>22</sup> The need for discipline was pointed out very early in the history of the USSC. They saw the need for expertness in key positions and the importance of compensation. They saw the flaws in "orgies of sentimental philanthropy." As pointed out in this article, they insisted on all persons submitting to discipline, whether paid or not. "A sound judgment, unaffected by mere sentimentalism or unsuspecting tenderness of heart, and most certainly free from all desire of parade and show—a sound judgment, I say, conjoined with an earnest sympathy with real suffering."<sup>23</sup>

Harriett Bartlett stated

There are two great channels for helping as social workers in the medical setting: (1) offering direct services to individuals and (2) helping the agency to meet the social needs of the people more responsibly and adequately.<sup>24</sup>

Nothing could better summarize the efforts of the Special Relief Department of the USSC.

Now let us turn to *A Statement of Standards To Be Met by Medical Social Service Departments in Hospitals and Clinics* prepared by the American Association of Medical Social Workers,<sup>25</sup> and analyze this statement on the nature of social case work.

*"Social casework in a hospital or clinic is concerned with helping the patient with personal or environmental difficulties which predispose toward illness or interfere with obtaining maximum benefits from medical care"*<sup>26</sup> In a crude way, one is inclined to say that this describes the work of the hospital visitors, but it wasn't consciously focused or as discretely considered as this statement suggests. They met needs of persons in hospitals; the subtleties likely escaped them.

*"This service depends upon individualized study of the patient so that his medical situation and its interrelationship with his personal needs and problems may be understood"*<sup>27</sup> This was

done but hardly with the calculated scientific consistency aimed at in today's practice

*Sharing of information between the doctor and the social worker is basic to their individual understanding of the patient* This has been established as being hospital visitor practice

*"With this understanding the caseworker helps the patient participate in a plan consistent with the medical recommendation and acceptable to him"* Evidence of this is an instance of a hospital visitor helping a patient accept the doctor's recommendation that he not go home but rather that he remain and have his mother come to the hospital

*The study of the patient and the help that is given him proceed concurrently Interviews with the patient and members of his family and conferences in his behalf with professional persons are the principal methods used The patient and his family are able to discuss their difficulties with the caseworker as they develop confidence in her and recognize her ability to help* This scarcely needs elaboration here The hospital visitor did talk with patients did plan with patient and relative They offered a personal service a daily and hourly intercourse which entered into his life and supplied his particular need

*Casework services may range from giving concrete suggestions for dealing with a simple problem to helping with such problems as fears of permanently disabling illness distress over disfiguring handicaps anxieties stemming from previous experiences which may be retarding recovery and plans for an uncertain future* The range of simple services has been described A case of a disfigured married soldier who was faced with death illustrates more intensive work The soldier wanted to see his wife and child (born since his leaving) but could not permit himself to be seen in his disfigured state With the help of the hospital visitor he was able to write to his wife Following the reply he could accept her coming Although very shaken at the prospect he found strength to see her She remained with him until his death

*The resources of the patient and his immediate environment are primarily used in giving help and frequently these are supplemented by the use of community facilities* This needs no further elaboration

*The quality of casework services is measured neither by its duration nor its complexity but by the evidence of recognition of human beings as individuals each reacting to a given situation according to his own needs and with a right to determine for himself the solution to the problems it may present for him* In individualization there was and there is no evidence in the prac

tree of the hospital visitor of denying the patient his right to determine his own destiny

## SUMMARY

While the Special Relief Department program resembles present day social services provided for soldiers, both as to philosophy and objectives, the professional equipment of the Special Relief agents cannot be compared with modern social casework skills. The absence of insight into human behavior provided by modern scientific understanding and skill in the use of relationship is evident in the methodology employed by Special Relief agents; however, in their regard for human dignity, concern for individual needs, and their general democratic attitude, there is evidence of similarity to current social work philosophy. The evidence would seem to indicate that modern military medical social work in the United States Army had its beginnings in the hospital visitor program sponsored by the Special Relief Department of the United States Sanitary Commission during the period 1861 to 1865.

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### MEDICINE IN THE REVOLUTIONARY WAR

It has been believed by some that American medicine benefitted materially through its Revolutionary War experience. I find it difficult to justify such a conclusion. Brook Hindle, a recent thorough investigator of the revolutionary period, has clearly shown that scientific enterprises generally suffered during the years of the conflict. He agrees that although the stature and status of the profession were in some respects enhanced by reason of its wartime activities, scientific medicine was not notably advanced during these years. Physicians were brought together from various communities on a scale not previously experienced. Furthermore, they treated traumatic injuries in large numbers and had abundant opportunity to make some progress in epidemiology and hygiene. Although some sound principles were enunciated, the record of the profession is not distinguished by originality or far-sighted progress.

—WILLIAM F. NORWOOD, Ph.D.  
in *Internat'l R d / M d i c i*  
p 400 J l y 1958

### THE IMMEDIATE IN TERMS OF THE ULTIMATE

A mature person thinks of the immediate in terms of the ultimate. This is the basis of good living, principles and sound surgical judgment. The present or the immediate has too often proved itself a jailer of our minds. It holds us captive. We live under the tyranny of a present incident and for this reason may react at times in very immature ways. A surgeon should have the bearing of maturity and one way of achieving this maturity is to think of the immediate situation in terms of the ultimate goal.

—LEONARD D. HEATON, M.D.  
i *Surg ry Gynec l gy & Ob tetric*  
p 484 Ap l 1958



## Clinicopathologic Conference

U S Air Force Hospital Parks Air Force Base, Calif \*

### DYSPNEA IN INFANCY

**Summary of Clinical History** This female infant was born on 22 December 1955, the third child of a 22 year old para 3, gravida 3 Negro woman. The pregnancy had been uncomplicated and the delivery was spontaneous. At birth the infant weighed 7 lb 12 oz and measured 21 inches in length. She appeared normal in all respects and was taken home on the fourth day after birth.

#### FIRST ADMISSION

The infant was admitted to this hospital on 10 February 1956. She had been in apparent good health until two days prior to admission when the mother had noticed that she had a high pitched and hoarse cry. On the day prior to admission the mother noted the onset of rapid respirations. The patient was brought to the outpatient clinic where a nasopharyngitis was diagnosed and the patient was given penicillin and streptomycin sulfate. The rapid respirations continued, however, and the fluid intake was markedly decreased so that the child was admitted.

**Physical Examination.** On admission the infant was lethargic and only fairly hydrated. Respirations were shallow and rapid, 60 to 70 per minute. No rales were heard but there was a slightly prolonged expiration over the left anterior chest. There was no cyanosis. There was moderate substernal and intercostal retraction. The heart rate was 200 per minute with a gallop rhythm. There were no murmurs. The liver was enlarged down to the level of the umbilicus. There was no pulsation of the liver.

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Col J h W L festy USAF (MC) Command From th Labor t ry S rvce M J  
Rob rt E Pl USAF (MC) Ch f

**Laboratory Examination** The white blood cell count was 10 800 per  $\mu$ l with 1 band form 49 segmented neutrophils and 50 lymphocytes Hemoglobin was 9.8 grams per 100 ml There was moderate to severe hypochromia anisocytosis and poikilocytosis The urine was yellow and cloudy with an acid reaction A slight trace of albumin was present and there were 10 to 15 white blood cells per high power field

A roentgenogram of the chest on admission revealed a considerable enlargement of the cardiac shadow predominantly to the left The vertical measurement of the heart was suggestive of true hypertrophy Pulmonary vascular shadows were increased bordering on congestion

The electrocardiogram on admission revealed an abnormal tracing with inverted T waves over the entire left precordium (leads AVL V<sub>1</sub> V<sub>2</sub> V<sub>3</sub> and V<sub>4</sub>) This was interpreted as compatible with a myocarditis or ischemia of the left ventricle

**Course: Hospital** Upon admission the infant was placed on digitoxin by intramuscular injection the total digitalizing dose being 0.025 mg per pound of body weight one tenth of this being for daily maintenance dosage A salt free diet consisting of Lonalac (brand of powdered food similar to whole powdered milk but almost free of sodium) was given Thiomerin (brand of mercaptomerin sodium) 0.5 ml was injected intramuscularly and 297 m<sub>u</sub> (300 000 units) of procaine penicillin G and 0.25 grams of streptomycin sulfate were given daily

During the hospitalization the infant's temperature varied from 91.6 to 100.4 F Twelve hours after the initial digitoxin was given the infant's liver had markedly decreased in size and the gallop rhythm had disappeared The heart rate slowed and after three days of therapy the infant appeared normal in all respects Repeated electrocardiograms revealed a rapid return to normal of the previous abnormalities thought to be due to myocarditis and electrocardiogram on 16 February was essentially normal

On the 11th hospital day intramuscular administration of digitoxin was discontinued and the infant was started on oral elixir digoxin with a maintenance dosage of 2 ml per day The child was discharged on the 13th hospital day to be followed in the outpatient clinic

On admission on 10 February the infant's weight was 9 lb 3 oz the discharge weight was 9 lb 1/2 oz

The child was seen in the outpatient clinic on 31 March because of a cough which had been present for two days At this time she weighed 10 lb There had been occasional regurgitation of food The roentgenogram at that time showed an enlarged heart with an otherwise normal appearing chest Procaine peni

cillin G, 297 mg (300 000 units), and 0.25 grams of streptomycin sulfate were given daily for three days. At the end of therapy the infant was much improved. The digoxin was continued.

The infant was again seen on 20 April in the outpatient clinic. She weighed 11 lb 9 oz, had been doing well, and there were no changes in the physical findings. At this time the first diphtheria pertussis typhoid vaccine injection was given.

#### SECOND ADMISSION

The infant was readmitted to this hospital on 4 May. For two days prior to this admission she had become progressively dyspneic, developed fever and vomiting, and the mother thought that the child had lost weight.

**Physical Examination** The infant weighed 11 lb. Her temperature was 102°F. She appeared moderately dehydrated. There was prominent subcostal retraction with moderate dyspnea and respirations were 60 per minute. The cardiac dullness extended to the left axillary space. No murmurs were heard. The cardiac rate was 180 per minute. There were expiratory wheezes over the entire chest. The liver was down two fingersbreadth below the right costal margin. A large umbilical hernia was observed.

**Course in Hospital** Therapy on admission consisted of Lytren (brand of complete electrolyte preparation for oral use) feedings every 3 hours, oxygen with Alevaire (brand of sterile aqueous solution containing the detergent superinone with sodium bicarbonate and glycerin), digoxin, aminophylline suppositories, 1/6 grain for wheezing, Terramycin (brand of oxytetracycline hydrochloride), 50 mg intramuscularly every 12 hours, and dextrose in water subcutaneously.

The infant appeared improved and there was a decrease in respiratory difficulty. On the third hospital day it was noted that she was much improved and the lung fields appeared clear. The heart rate was 160 per minute at this time.

The same evening she was coughing, choking, and crying. She was suctioned with a bulb syringe and much mucus was obtained. Following this she became more quiet and somewhat drowsy. At 2300 hours she was again coughing and respirations were labored and rapid, 72 per minute. Temperature at this time was 102.4°F. She was given 0.05 mg of digitoxin intramuscularly at 0200 hours, 7 May. One half hour later an aminophylline suppository was given per rectum. Following this the infant became quieter and the respirations were less labored. She awoke at 0430 hours and was crying weakly and coughing. Temperature at 0610 was 101.2°F. She died quietly at 0612 hours.



## DISCUSSION

**D to Barki** The CPC today is on the discussion and differential diagnosis of congenital heart defects. This is becoming an increasingly important topic because of the spectacular advances in correction of heart defects and the fact that 2 out of 100 people are affected.

The patient was a female infant, the third child of a 22 year-old para 3 gravida 3 Negro woman. The pregnancy had been uncomplicated and the delivery spontaneous. The infant's weight, length, and appearance were normal for the first four neonatal days.

This brings up the question of the cause of congenital heart defects.<sup>1</sup> The only condition definitely known to produce a congenital heart defect is German measles during the first three months of pregnancy. This is something that can be prevented by your little girls having German measles while they are little girls. Should the situation occur that the wife develops German measles during the first three months of pregnancy, she may well realize from reading lay journals that she is carrying a child that will have a one out of five chance of having a congenital heart defect. This is not conducive to a happy pregnancy.

The other conditions that produce congenital heart defects have just been performed in experimental animals. Vitamin A or vitamin E deficient rats have been found to have litters with a higher percentage of congenital heart defects. An experiment was performed in which female rats were placed in a drum 18 inches in diameter and it was spun for 40 revolutions a minute for 300 revolutions between the eighth and thirteenth gestational day. The percentage of congenital defects in these litters was 85 per cent as opposed to the normal occurrence in rats of congenital heart defects of about 2 per cent. Such stress situations in humans would be hard to imagine.

ACTH and cortisone will produce a greater number of congenital heart defects in mice. This has not been duplicated in any other experimental animals.

The question of whether or not hypoxia can produce congenital heart defects was studied. A hypothetical case of a possible knot in the cord during the development period in the embryo can be suggested as the cause of congenital heart defect but there has been no evidence of it. There are different teratogenic agents like trypan blue and triethylenemelamine known to produce congenital heart defects. At the present time, except for the question of irradiation where experimental animals also have a greater number of congenital heart defects, German measles is the only condition known to definitely produce congenital heart defects in the human.

The patient was admitted to the hospital at the age of 7 weeks. She was brought into the hospital because of nasopharyngitis, a rapid respiratory rate, and she was in heart failure with a heart rate of 200 per minute. The liver was enlarged to the level of the umbilicus.

The laboratory data revealed an increased number of neutrophils over the normal number for a 7 week-old child and the hemoglobin was a little low with a moderately severe hypochromia so that there was a possibility that this child had an iron deficiency anemia due to the fact that the mother was deficient in iron during the pregnancy. A slight trace of albumin was present in the urine. This frequently occurs in a patient with congestive heart failure.

X-rays of the chest revealed a considerable enlargement of the heart shadow predominantly to the left. This signifies a left and/or right-sided enlargement of the heart. It was interpreted as suggestive of true hypertrophy, and this is unusual as few radiologists will make such a statement from looking at an x-ray. Pulmonary vascular shadows were increased bordering on congestion. This is a very important point to observe in placing congenital heart lesions into various categories. The fact that the child was in failure doesn't give this x-ray too much meaning. If the child were not in failure one would look closely at the pulmonary vasculature to see if it were increased, normal, or decreased. This doesn't always place us in the correct category, and the reason for that is the knowledge of what happens to the pulmonary vasculature under stresses of congenital heart lesions. At birth the size of the lumen of the pulmonary arteriole is normally one-half that of the diameter of the musculature. When the child takes his first breath and the alveoli begin to open, the lumen of the pulmonary arteriole also increases in size and the ratio becomes greater than that of the musculature. In one month the lumen of the arteriole becomes three times the size of the musculature, and in the adult the lumen is five to six times the size of the musculature.

There are three things in congenital heart defects that affect the pulmonary vasculature. One of these is the ejective force of the stream upon the pulmonary bed. The ejective force is defined as the flow of blood that is produced through a ventricular septal defect that is greater than 40 per cent the diameter of the aortic orifice. This defect, of course, produces the greatest stress on the pulmonary bed. The second factor that affects the pulmonary vasculature is increased blood flow. This is present in many congenital lesions in varying degrees: the atrial septal defect, anomalous pulmonary drainage, patent ductus, and several others. The third factor is the back pressure produced by obstructive lesions distal to the pulmonary flow, such as mitral stenosis.

Normally the pressure of the blood going through the pulmonary system is only 20 to 25 per cent that of the systemic blood flow. In cases such as an interventricular septal defect where the blood is pushed through under greater pressure the lumen increases in size,

the left side of the heart has to work harder to draw off this extra amount of blood in the pulmonary system and the pressure in the pulmonary system may go up to equal the pressure in the systemic system. This would of course produce the greatest stress on the pulmonary vasculature. In this event either the nervous system responds by constricting the lumen of the pulmonary vasculature thereby decreasing the pressure of the pulmonary system relative to the systemic system or the muscle of the arteriole hypertrophies and there is intimal proliferation to produce greater resistance in the pulmonary vasculature. The other chance in a large ventricular septal defect is that the right would increase in size while the ventricular lesion would remain about the same size becoming smaller than 40 per cent of the size of the diameter of the aortic orifice. There the ejectile force factor would be no longer present and there would be less stress on the vessels of the pulmonary bed.

The vasculature is described in three phases: (1) the normal evolutionary pattern with the increasing size which I have described; (2) the muscle hypertrophy and intimal proliferation; and (3) an irreversible change in the pulmonary bed. This has the greatest effect on the prognosis of the patient. Some conditions produce these changes more profoundly than others. With an interventricular septal defect the changes may be irreversible in the first year. In a large atrial septal defect there may be no change in 20 years of life. With a malocclusive pulmonary drainage change may occur in the first few years of life. So it depends upon the type of congenital heart defect how early one must consider these pulmonary vascular changes and how rapidly an operative procedure must be performed. Of course, very conditions vary with the latitude and relative increase in blood flow.

The electrocardiogram interpreted as compatible with myocardial infarction of the left ventricle. This gives us the category to which the patient most probably fits. She is a cyanotic child who has a murmur and one in whom the left ventricular involvement probably is primary.

The five congenital heart defects plus acute myocardial infarction frequently confused us in diagnosing such a congenital heart defect. The most common condition in this category is primary endocardial fibroelastosis. This is a condition that constitutes 7 per cent of all major heart malformations. Here there is a fibroelastic thickening of the endocardium with pressure upon the Thebesian vessels with decreased flow of blood to the muscle producing left ventricular ischemia.

The other conditions are: 1. Glycogen storage disease. This is a difficult one to rule out. It is caused by the deposition of glycogen in the heart muscle and it may produce ischemia. However, it is usually general and throughout the heart. 2. In some cases the left coronary artery arises from the pulmonary artery. Here with the decreased oxygen content and decreased flow through my blood for oxygenation the

heart muscle. Frequent ectopic is an anterior myocardial pattern on the electrocardiogram and there may be dilatation of the right ventricle. 3 Sometimes the coronary arteries are lined with thrombus giving signs of cardiac insufficiency. 4 A rhabdomyoma of the ventricle can produce a large heart, and this must be included in the differential diagnosis.

Myocarditis is the more common situation to be brought to mind like this to be differentiated from fibroelastosis. Frequent differentiation is by the response to digitalization. As we saw in the discussion the child was placed on digitalis and responded in a 12 hour period. This is a good point favoring one of the defects over myocarditis. The digitalizing dose of digitalis in this case was 0.025 mg per pound of body weight. A study of digitalizing doses at St. Louis Children's Hospital showed that 0.035 mg per kg of digitalis did not seem to produce any more deaths than 0.035 mg per kg.<sup>2</sup> This was certainly a good digitalizing dose for this patient. A salt free diet, mercurial diuretics, and also were used. Within three days the child appeared normal on examination with electrocardiographic findings returning to normal. The change of the electrocardiogram to normal would be in favor of myocarditis.

The patient developed a second upper respiratory infection and responded rapidly to streptomycin sulfate and penicillin. It was noted at this time to be enlarged with an otherwise normal appearing chest. We deduce from this that there was probably a normal pulmonary blood flow. The enlarged heart does not indicate that there was any particular change in enlargement or whether it was left or right-sided enlargement.

At four months of age this child weighed 11 lb 9 oz. At four months a child usually has doubled his birth weight, while this child is a little underweight. This child of course has had respiratory infections and episodes of heart failure.

The patient was readmitted at four and one half months with an episode of asthma which threw her into a second episode of congestive heart failure. Infection appeared to predispose to the asthma. The treatment was complete and the child died on the second day of hospitalization, however because of the throat coughing and choking occurred and this threw the child into cardiac failure and caused her death.

In the differential diagnosis of this condition in the acyanotic child with no murmur are there any procedures that have been done to further differentiate the congenital defects? An anomalous pulmonary vein could produce a similar picture except that there would be right ventricular hypertrophy. Differentiating point between the five conditions that I have mentioned is anomalous pulmonary drainage. To find out before the patient if this condition exists an angiocardiology procedure

but here it would only help if the pulmonary vein drained into one of the larger veins such as the inferior or superior vena cava and we were lucky enough to have some dye going into the pulmonary vein. Frequently there is an atrial septal defect associated with the anomalous pulmonary vein but in view of the repeated statement that there were no murmurs this does not appear to have been present

Glycogen storage disease may be shown by the presence of increased amounts of glycogen in muscle at biopsy. However this may not be positive. The other tests that will tell us if the patient has glycogen storage disease of the liver type do not apply to the cardiac type. In the patient with storage of glycogen in the liver there appears to be an absence of glucose-6-phosphatase and the patient cannot change glucose to glycogen or glycogen to glucose therefore there is a low fasting blood sugar and frequently acidosis and ketonuria because of the breakdown of fats to supply energy. There may be a blood lipid level of up to 5 mg per 100 ml. When a glucose tolerance test is made in these patients the glucose is high because it isn't converted to glycogen. These tests do not apply to the cardiac type of glycogen storage disease. In the case of the left coronary artery arising from the pulmonary artery there is no good diagnostic finding except for the presence of an anterior myocardial infarction pattern on the electrocardiogram. The other condition rhabdomyoma would just be found at autopsy. We would tend to rule out myocarditis because of the patient's rapid response to digitalization.

And so favoring the more probable and common lesion my feeling is that on autopsy of this patient we would find a primary endocardial fibroelastosis.

In fibroelastosis as well as in cases of left coronary artery arising from the pulmonary artery a surgical procedure that has been suggested is to put talcum on the pericardium in an attempt to increase the collateral circulation. Several patients reported on in the literature have been doing well two to three years after this surgical procedure.

Doctor Paul White reported some adult cases of fibroelastosis and in similar situations where they have tried to relieve coronary insufficiency in adults it has not been too successful.

There are two main types of fibroelastosis one of a dilated heart the other a contracted heart. In the dilated heart which forms the majority of cases the left ventricle and left atrium are the two chambers most often involved although occasionally the right ventricle may be affected. In a fair number of cases 10 to 20 per cent the mitral valve will be involved so that a child with a murmur in this region would not rule out fibroelastosis.

Dr. B. G. D. The initial postero-anterior chest film on this child (fig. 1) shows a rather marked enlargement of the cardiopericardial

silhouette. This enlargement is of a diffuse globular nature. There is in addition a considerable accentuation of pulmonary markings bilaterally. We take this to be evidence of congestion and cardiac failure. In view of the generalized enlargement of the cardio-pericardial shadow, I do not believe we can comment accurately on specific anatomic changes.



Figure 1 Initial chest film showing enlarged heart and accentuated pulmonary markings.

The next chest film was obtained during the patient's initial hospitalization and after digitalization. Again we see an enlarged globular heart with increased pulmonary vascularity. The child was fluoroscoped at this time and the fluoroscopist reported no specific changes. He did note that there was, throughout the cardio-pericardial silhouette, a diminution of the amplitude of pulsations. Apparently there were no specific changes at this time to suggest a pericardial effusion to the fluoroscopist. Hence from this point we will assume that this is cardiac enlargement and that there is no pericardial effusion. As Dr. Barkin has pointed out, we make no attempt to differentiate between cardiac dilatation and hypertrophy. In my opinion

difference in the appearance of these processes radiographically and frequently both processes are present simultaneously

The third chest film on this child is dated 5 March 1956 at which time the child was considerably improved clinically. There has been considerable improvement in the appearance of the chest as well. The heart is still quite large but is perhaps a bit smaller than on our previous film studies. Certainly the patient appears much better compared to the time with the pulmonary markings approaching normal. The liver shadow is also somewhat smaller than on earlier films.

The final chest film (fig. 2) shows the enlarged heart with the left border projected all the way out against the left lateral thoracic wall.



Figure 2 Final chest film showing enlarged heart and prominent left lateral shadow.

Once again the child appears to be in full recovery with a marked prominence of the shadow in the right lung field. The left lung field is for the most part obscured by the cardiac silhouette.

In summary the findings are these (1) a very large globular heart which progressively enlarges but in which there are minimal changes from time to time (2) episodes of failure and of compensation (3) an acyanotic child (4) no significant murmur (5) repeated bouts of upper respiratory infection (6) a child who was apparently normal at birth and shortly thereafter

I would agree with Doctor Barkin in that I doubt that this falls within the acyanotic or cyanosis tardive types of congenital heart disease. In such cases there ordinarily is not as massive enlargement of the cardiopericardial silhouette and in most instances there are rather typical murmurs. In addition in many of the acyanotic types there are specific anatomic changes which are apparent radiographically.

I believe that this most likely represents a case of endocardial fibroelastosis. Roentgenologically one cannot differentiate this disease from glycogen storage disease of the heart. However it is my impression that in glycogen storage disease the heart will not respond as readily to digitalis therapy and that it does not show as much change from film to film.

Doctor Barkin: Do you think that barium by mouth would have helped to show if the left auricle was enlarged?

Doctor Brogdon: Actually this patient was given barium at the time of fluoroscopy referred to previously; this did not contribute any additional information. The left atrium was enlarged but not inordinately so. All chambers appeared diffusely enlarged. Ordinarily any attempt to demonstrate specific chamber changes in the massively enlarged failing heart is fraught with difficulty.

Doctor Worthman: In the standard leads of the electrocardiogram (fig 3) there is not the degree of right axis deviation that I would expect in a child of just a few months of age. The QRS complex in II and III are primarily upright and in lead I there is a small S. In aVR there is a small R. If there were a right ventricular predominance one would expect a tall R and R in lead aVR. The rather prominent QRS in aVF lead and an R equaling the S in aVL throws it pretty much into a vertical or semivertical position which is the position one would expect in this age group. In the precordial leads we have a tall initial R in  $V_1$  with an S of about a third the size. Progressing to the left side there is not a great deal of change. On the left side there is still a rather tall R with an S of about a third the size of the R. The T waves are more inverted as we get over on the left side than they are on the right. This is somewhat opposite to the pattern seen normally wherein the T waves are inverted in leads  $V_1$ ,  $V_2$ ,  $V_3$ , and even  $V_4$ , tending to become upright in  $V_5$  and  $V_6$ . There is some elevation of the S-T segment on the left side starting about  $V_4$ , which looks significant. In essence it looks to me as though there is evidence of strain if you will accept



the term on the left side as manifested by less right axis than I would expect and the ST segmental and T wave changes over the left precordium

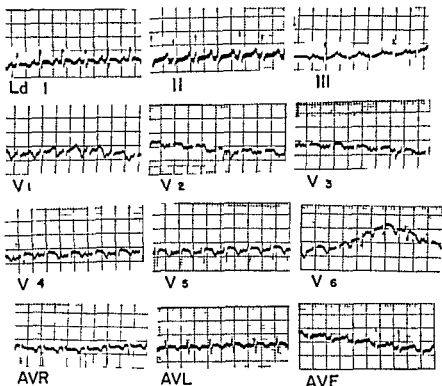


Fig 3 Initial electrocardiogram.

In the next electrocardiogram (fig 4) following treatment there has been some change in that the ST elevation doesn't seem to be apparent at all. This segment is isoelectric. The T wave is upright in V<sub>1</sub> apparently upright in V<sub>2</sub> and in V<sub>3</sub>. Another feature here is that the voltage of the QRS is small in V<sub>1</sub>. In general I think that this would go along with improvement in the status of the left ventricular musculature in a rather nonspecific way. I can't really account for the low voltage in V<sub>1</sub>.

Dr B Kin's diagnosis

Congenital heart disease, probably endocardial fibroelastosis

Dr Bogdan's diagnosis

Endocardial fibroelastosis

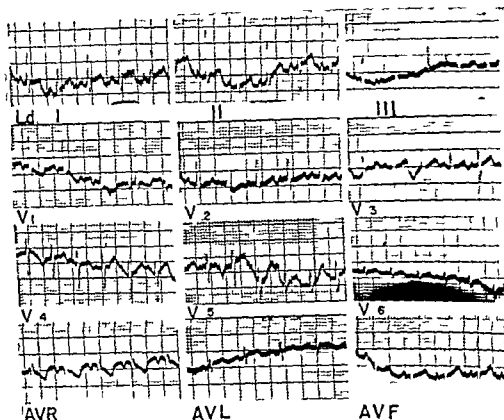


Fig re 4 Electrocardiogram following *d* gitalization.

#### PATHOLOGIC FINDINGS

Doctor Ple cer At autopsy the body was that of a fairly well developed and well nourished Negro female infant which demonstrated a moderate degree of dehydration. A small reducible umbilical hernia was present.

The lower edge of the liver was about 3 cm below the right costal margin in the midclavicular line. About 5 ml of clear amber fluid was present in each pleural space. The heart was markedly enlarged, taking up an estimated one third of the entire thorax. The left lung was compressed and there was a mild mediastinal shift to the right side.

The right lung weighed 98 grams, the left 49 grams. There was compression atelectasis of the left lung.

The heart weighed 87 grams, as compared to an expected normal of about 60 grams. This enlargement was due principally to left ventricular hypertrophy. The principal gross abnormalities were in the left ventricle. The endocardium of the entire left ventricle (fig 5) including the papillary muscles was opaque gray white and averaged 1 mm in thickness. This change did not include the valves. All chambers of the heart were slightly dilated, but to a much lesser degree than the left ventricle. The coronary arteries had a normal origin, appearance, and distribution.

The liver weighed 200 grams (the very upper limit of normal) and was normal in shape and consistency. The cut surface showed light tan liver tissue with fairly prominent markings.

The other organs were grossly normal.



Fig. 5. V. of the pen d l f t e n t l l o u g t h t h k d d o a r d u n.

Microscopic examination of the left ventricle (fig. 6) showed prominent fairly uniform thickening of the endocardium due to increased connective tissue. There was prominent collagen formation associated with the increased fibroblasts. Special stains (fig. 7) also demonstrated the increase in the elastic fibers. In rats there were extension of the fibroblasts into the adjacent myocardium. The myocardium showed hypertrophy.

The gross and microscopic findings are characteristic of so-called endocardial fibroelastosis. The manner of death is attributed to a rather acute cardiac failure secondary to the cardiac insufficiency produced by the endocardial fibroelastosis.

The clinical entity was first named endocardial fibrosis by Weinberg and Hamefarb in 1943. It is characterized by a non-inflammatory fibrosis of the mural and valvular endocardium, particularly in the left cardiac chamber. Usually both aortic and mitral valves are involved and often the myocardium is hypertrophied. Occasionally the right side of the heart dilates and hypertrophies. Congenital defects are often found such as aortic hypoplasia, transposition of the great vessels, patent ductus arteriosus, and patent foramen ovale.

Clinically the infants are normal at birth. The onset of signs or symptoms is sudden. Cough is the common symptom. Irritability, no exertional dyspnea, and cough are frequent. Physical examination shows signs of congestive heart failure. The heart may or may not be enlarged and usually a prodromal systolic murmur has occasionally a

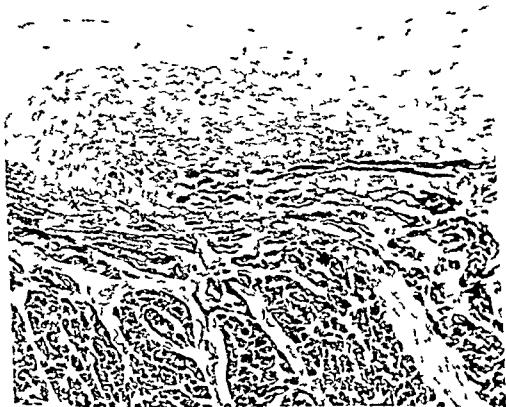


Figure 6 Photomicrograph of left ventricular endocardium showing marked fibrous thickening (hematoxylin and eosin stain  $\times 100$ )



Figure 7 Photomicrograph demonstrating increased elastic fibers (Verhoeff's elastic stain  $\times 150$ )

diastolic one is also present. After the clinical picture develops the duration of life is often short usually not more than 10 days. The average age at the time of death is 4 to 6 months.<sup>6</sup> Left ventricular failure is the most common cause of death.

The left side of the heart especially the left ventricle is involved more often and more severely than the right side. The endocardial thickening may be diffuse in the left ventricle and patchy in the other chambers or diffuse throughout the entire heart. Deformities of the mitral and aortic valve are present in about 50 per cent of cases while involvement of the pulmonary or tricuspid valve is less frequent.<sup>7</sup>

The cause of the condition is unknown but many varying factors have been proposed. The possible role of maternal toxemia and infection has been widely discussed. The evidence in favor of an intra-uterine infection is not convincing. There is little histologically to support an infectious basis. The lesions are conspicuously free from inflammatory cells. Only one case of fibroelastosis associated with rubella in the fourth month of pregnancy has been reported. Weinberg and Himelfarb reported two siblings the second and third pregnancies with this entity. Those pregnancies were both uneventful.

In those cases associated with aortic valve lesions or coarctation it has been suggested that the myocardial and endocardial thickening represent hypertrophy caused by increased work. Another suggestion is that the endocardial thickening might result from the organization of mural thrombi. However such lesions are different from the smooth diffuse thickening found in fibroelastosis. Also the intermediate stages in the process of organization are not observed.

Still another suggestion has been made that fibroelastosis should be classed with the collagen diseases. Nothing resembling fibrinoid has been found and there is no other similarity of this disease to the recognized members of the collagen disease group.

Most recent authors have taken the view that fibroelastosis represents a primary abnormality of fetal development an endocardial dysplasia of unknown cause. In the present stage of knowledge it would seem impossible to go further than this.

There have been several reports of diffuse endocardial sclerosis in adults. Grossly there is some resemblance to the infantile lesion but it is considered that the two conditions are not related.

#### Pathologic diagnosis

##### 1 Endocardial fibroelastosis with myocardial failure

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### SOLDIERS AND LABORATORY ANIMALS

No military commander is entitled to subject his men to risks and sufferings which he himself would not be prepared to endure if *mutatis mutandis* circumstances required him to do so. We may bear in mind also that circumstances do not ordinarily require a divisional commander to expose himself to the same risks as the front line troops however often he may have done so in his younger days his duty is now different from theirs. But in principle he ought to be ready to face anything he calls upon them to face. If we turn now to the biologist we may say that only in rather exceptional cases can he usefully subject himself to experimental procedures in the laboratory though a number of research workers have done this from time to time. On the other hand he may usefully ask himself whether if he were this or that experimental animal he would be willing to make voluntarily the sacrifice which he is calling on the animal to make for the sake of the purpose for which the experiment is to be performed apart always from any question of life and death and account being taken only of any pain, discomfort or stress that may be entailed.

—C W HUMPHREY, M.A., M.C.  
in *Lancet*  
p 426 Feb 22 1958

## CASE REPORTS

### Thrombophlebitis and Vertebral Osteomyelitis in an Infant

MANARD E. PONT *Captain USAF (MC)*

**T**HROMBOPHLEBITIS is a disease so uncommon in infants that it is not mentioned in the standard textbooks of pediatrics. It is seen almost exclusively as a complication of such procedures as venous catheterizations in cut downs or secondary to venous stasis resulting from occlusion of large veins as by a large retroperitoneal tumor.

Acute hematogenous osteomyelitis on the other hand is considered a rather common disease of childhood although its incidence has decreased markedly since the introduction of antibiotic therapy on a widespread scale. This decline is said to be the probable result of the frequency of antibiotic treatment in such conditions as respiratory infections, cellulitis, and boils which are considered to be the precursors of acute hematogenous osteomyelitis. The disease which is secondary to a bacteremia was classically described as being caused by *Micrococcus pyogenes* var. *aureus* (*Staphylococcus aureus*) in the majority of cases although *Streptococcus hemolyticus*, *pneumococcus*, and *Escherichia coli* (*Bacillus coli*) were considered to be common etiologic agents. Within recent years there have been an increasing number of case reports indicting the gram negative organism of the salmonella group as the etiologic agent.

The disorder involves a primary lodgment of organisms in the metaphysis, the cancellous bony portion adjacent to the epiphysis of a long bone. The organisms then spread into the medullary cavity through the Haversian canals into the subperiosteal spaces. Bone necrosis and the formation of sequestra are the common sequelae of this process. Vertebral osteomyelitis differs from the osteomyelitic process in the long bones however in (1) the absence of sequestra formation and (2) a characteristic massive new bone formation which occurs early in the process. Collapse of the vertebra is less common than might be imagined because the severity of the pain usually forces the patient to lie recumbent from an early stage of involvement.

The clinical picture of acute hematogenous osteomyelitis is highly variable some cases demonstrating a high degree of systemic signs and toxicity, while others show almost no systemic involvement whatever. Of interest in our case is the statement of Blanche<sup>7</sup> that infants ordinarily tend to demonstrate few systemic signs, despite multiple foci of involvement.

### CASE REPORT

This male child was born on 8 January 1957 to a 44 year old woman, para 5 gravida 8 following an uneventful pregnancy and delivery. He weighed 6 pounds and 12 ounces. The post partum period in the hospital was uneventful except for a routine circumcision performed without anesthesia at the age of three days. On the day following circumcision the child was discharged from the hospital.

The child was not seen again until the night of 22 January, when he was brought to the hospital dispensary with a fever (103° F rectally) and the complaint that he kept his left leg flexed and refused to allow it to be extended as if it were very painful. At this time examination of the child revealed no physical findings except an evident tenderness of the leg and resistance to movement. The leg was not red, swollen or discolored. He was referred to the pediatric clinic where a tentative diagnosis of Caffey's disease (infantile cortical hyperostosis) was made. This is a syndrome characterized by subperiosteal calcification, soft tissue swelling, fever, local heat and tenderness and elevation of the serum alkaline phosphatase. When he was seen again four days later he was apparently doing well in that he had been afebrile. However he apparently still had a painful leg and cried loudly when it was moved. When he was seen again on 1 February the mother complained that the left lower leg was apparently larger than the right one and appeared to be darker. At this time the right calf measured 5½ inches and the left calf 7¼ inches in circumference.

On 6 February the child was admitted to the pediatric ward with a diagnosis of Caffey's disease. At that time he was moderately well developed, well nourished and weighed 7 lb 13 oz (a gain of 1 lb 1 oz in the one month since birth). He appeared to be healthy and examination of the eyes, ears, nose, throat, chest, heart and upper abdominal region were negative. However the left lower quadrant of the abdomen, the left side of the scrotum and pubic region were markedly edematous. Marked venous distention was seen over the left lower quadrant. The left thigh was markedly swollen and reddened and there was a deeply cyanotic cast to the lower part of the left leg. Pitting edema was present to plus 2 or 3 below the knee. The patient had a temperature of 101° F rectally. The admission blood studies revealed a white cell count of 20,350 per  $\mu$ l and a hemoglobin of 11.8 grams per 100 ml. Urinalysis revealed 8 to 10 white blood cells per high power field. The throat culture contained hemolytic *M. pyogenes* var. *aureus* (80 per cent). Repeat white blood cell and differential counts on 10 February revealed 15,000 cells per  $\mu$ l with 66 per cent neutrophils.



25 per cent lymphocytes 6 per cent monocytes and 3 per cent eosinophils. A blood culture drawn at the time of admission revealed non hemolytic coagulase positive *M. pyogenes* var *aureus* sensitive to bacitracin chloramphenicol streptomycin sulfate and erythromycin. All roentgenographic findings were normal at this time.

On the basis of the clinical and laboratory findings a diagnosis of thrombophlebitis of the left common iliac vein with septicemia of *M. pyogenes* var *aureus* origin was made. The patient was placed on a regimen of antibiotics and anticoagulants. This consisted of 150 mg (150,000 units) of procaine penicillin G intramuscularly every six hours and 50 mg of erythromycin by mouth every six hours. Depo Heparin Sodium was started on 7 February 16 mg every 12 hours with no apparent lengthening of the clotting time after 24 hours. On 8 February heparin sodium 10 mg every 12 hours was given later this was increased to 10 mg every eight hours. On 9 February the clotting time was 4½ minutes and it rose slowly to 6 minutes by 18 February. The dosage was decreased slowly to withdrawal from 18 to 23 February. Within two days after the beginning of this combined therapy there was marked subsidence of the edema apparent pain and immobility of the leg. On 16 February despite the subsidence of the pain and swelling and a decline in fever to normal the white blood cell count remained elevated at 21,700 per  $\mu$ l with 44 per cent neutrophils 55 per cent lymphocyte and 1 per cent eosinophils.

On 16 February a roentgenogram of the abdomen was suggestive of a mass in the retroperitoneal abdominal area which had been suspected as the cause of stasis in the venous system leading to thrombosis. A pyelogram on 18 February however did not reveal an abnormal mass within the retroperitoneal space (fig. 1).

Collapse of the body of the fourth lumbar vertebra was first noted on 26 February on routine roentgenogram (fig. 2). This suggested (1) metastatic malignancy (2) tuberculosis or (3) acute hematogenous osteomyelitis. On 2 March a roentgenogram of the chest revealed consolidation of the right upper lung field with scattered radiolucencies suggestive of abscess formation among the possible causes. Staphylococcal pneumonia was prominently considered. The roentgenogram of 6 March demonstrated collapse of the bodies of the fourth and fifth thoracic vertebrae (fig. 3) and there was the suggestion of a large mass to the left of the thoracic spine. At this time all blood cultures (except the nitrate one) urine cultures and spinal fluid cultures had been negative. On 6 March streptomycin sulfate paraminosalicylic acid (which was discontinued on 18 March) and isoniazid were started despite negative tuberculin skin test and no bacteriologic evidence of acid fast bacilli.

On 12 March a conference of the pediatricians radiologist surgeons and orthopedic surgeons determined that an exploratory laparotomy was indicated to investigate possibility of retroperitoneal mass and possible primary tumor. A retrograde pyelogram revealed essentially normal renal pattern bilaterally but the upper ureters somewhat

beaded and the middle third was displaced laterally on the antero-posterior and oblique views at the level of the collapsed vertebra. It was believed that the genitourinary tract in itself was normal.



*Figure 1 The pyelogram of 18 February 1957 showing a normal fourth lumbar vertebra.*

but that there was displacement of the ureter by a probable retro-peritoneal mass. It was thought that this space should be explored to establish a diagnosis for definite therapy. Because of the child's

condition this operation was delayed until 3 April by which time marked clearing of the lungs had occurred and there was general improvement in his condition.

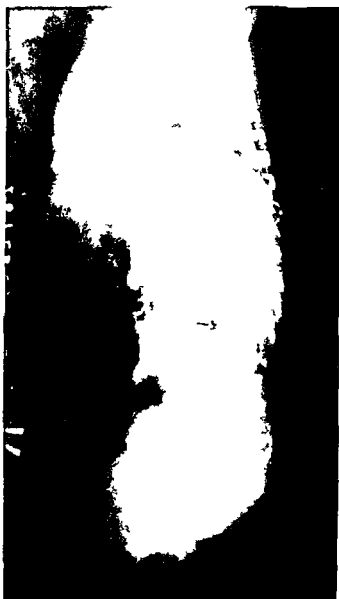


Figure 2. On 26 February 1957 collapse of the body of the fourth lumbar vertebra is demonstrated.

On 3 April following intravenous pyelography which neither substantiated nor ruled out a retroperitoneal mass the child underwent laparotomy. Through a left flank incision the peritoneum was reflected

anteriorly and the retroperitoneal space explored. The left ureter was adherent to the sigmoid colon. There were no masses along the vertebral column. The kidneys were found to be normal. The peritoneal cavity was explored through a small incision in the peritoneum and no abnormalities were found. The vertebral space was aspirated and 5 ml of bloody fluid was obtained. The fluid was found to be negative for bacteria, acid fast bacilli, and fungi. Postoperatively the patient did very well and symptoms of acute infection subsided.

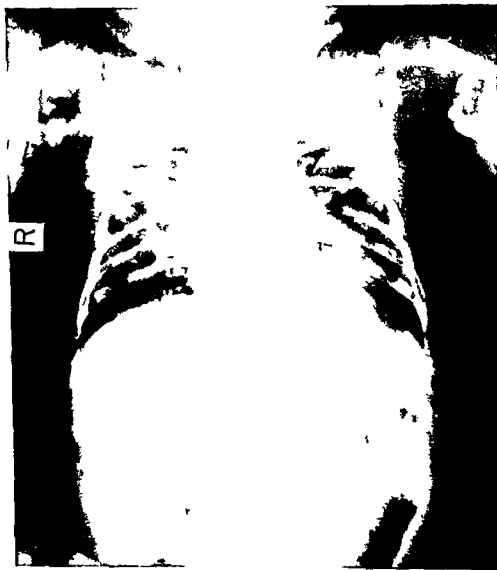


Figure 3 By 6 March 1957 the fourth and fifth thoracic vertebrae had collapsed and a bulge to the left could be seen. Some of the infiltrate in the right lung was still present.

On 13 April the child was discharged from the hospital. At this time he had developed to within normal limits and showed no signs of disease except for the three collapsed vertebrae. Early in May he was placed in a cast by the orthopedic surgeons for immobilization of the collapsed vertebrae. Erythromycin was substituted for chlo-

ramphenicol early in May 1957. The patient continued to be followed at monthly intervals. The erythromycin was discontinued at the end of August. The cast was removed in October. During this time remark-

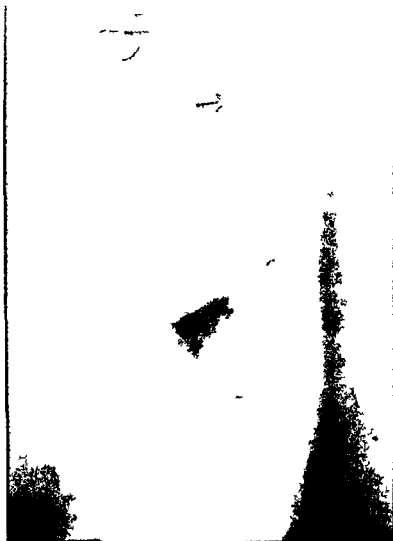


Figure 4. Radiogram made on 17 December 1957 showing good healing of the fracture of the lumbar vertebra. Callus also is present at the fracture site.

able healing of the collapsed vertebra was seen. The patient continued to develop and to gain weight and showed no evidence whatever of active disease. A roentgenogram on 17 December showed good

construction of the fourth lumbar vertebra and callus was present at the fourth and fifth vertebrae (fig 4)

### DISCUSSION

Within recent years staphylococcal infections have assumed an increasing importance among the diseases of early infancy. It is likely that the dramatic and tragic nursery epidemics of staphylococcal infections have been a major factor in directing attention to this group of diseases. However, in addition, during an era when most infectious diseases, including tuberculosis, have responded to therapy, staphylococcal infections have become important because of their notorious development of resistance to the chemotherapeutic agents. The early infantile age group is remarkably susceptible to staphylococcal infections, both mild and severe. The mild staphylococcal infections, those of the skin and superficial organs (furunculosis, impetigo, conjunctivitis, omphalitis, and breast abscesses) are probably the most common infections of early infancy. These infections are important however mild they may seem, in that they serve as a mode of entry for staphylococci into the body; this entry may facilitate spread to the bloodstream, lungs, meninges or, rarely, bone. The early infantile age group seems particularly susceptible to staphylococcal infections of these organ systems, particularly of the lungs. Recent studies<sup>1,2</sup> have indicated that more than half the cases of staphylococcal pneumonia reported in the pediatric age group occur in infants under six months of age. These factors combine to make staphylococcal disease of prime importance in the pediatric age group.

Our case presented a difficult problem in differential diagnosis from the beginning. Following what is believed to be a completely normal delivery and puerperium, the child first showed evidence of illness at the age of two weeks, when he presented with fever and evident pain in flexion of the leg. At that time, the clinical picture of pain, immobility, and very slight swelling in the leg, suggested the possibility of a congenital disease, such as Caffey's disease. However, the development of the full blown picture of thrombophlebitis occurred so quickly and typically that the staff overcame their understandable reluctance to make a diagnosis of a disease so rarely found in this age group.

I can offer no hypothesis to account for the development of thrombophlebitis in this case. However, septicemia of the neonatal age group is not uncommon, and it is not unreasonable to assume that the staphylococcal septicemia may have been the result of contamination of the umbilical cord, or a furuncle on the skin which went unrecorded.

During the patient's hospitalization, many members of the staff believed that an abdominal mass would be found to explain the venous stasis which predisposed to thrombophlebitis. This

mass was never found and at no time in the extensive investigation which was undertaken was there found any clue as to the pathogenesis of the thrombophlebitis

The collapse of the three vertebrae occurring as rapidly as it did suggested three possibilities first a rapidly metastasizing malignancy We believe that a one year follow up with complete subsidence of all signs of the disease process has effectively ruled this out. The second possibility tuberculous osteomyelitis of the vertebral bodies was a heatedly contested diagnosis among the attending and consulting staff However, it was thought that the roentgenogram of the chest did not indicate tuberculous involvement of the lungs that the persistence of a negative tuberculin skin test over a one year period is almost mutually exclusive to such a diagnosis that the two-month period of antituberculosis therapy which this child was given was insufficient to arrest permanently the progress of such a disease that the inability to recover acid fast bacilli on repeated gastric aspiration blood cultures spinal fluid cultures, and even vertebral aspirations contraindicate this disease

The diagnosis of acute hematogenous osteomyelitis secondary to the staphylococcal septicemia seems to be the only other tenable diagnosis in this case First septicemia resulting from *M. pyogenes* var *aureus* was demonstrated by blood culture It was within a few days following this while the child was still febrile and had a marked leukocytosis that roentgenographic evidence of collapse of the body of the fourth lumbar vertebra was first seen The other two vertebral collapses occurred very quickly and cessation of the appearance of new vertebral collapse coincided with the decline in fever leukocytosis and evidence of toxicity The subsequent regeneration of bone on immobilization occurred during a period of intense antibiotic therapy directed toward the staphylococcal infection It is felt that these observations substantiate a clinical and laboratory diagnosis of acute hematogenous osteomyelitis secondary to staphylococcal septicemia

We wish to comment briefly on the difficulty encountered in the anticoagulation process and suggest that if the rarity of the disease makes diagnosis difficult it makes treatment even much more so

ACKNOWLEDGMENT The authors wish to acknowledge the contribution of Dr. Gordon D. Jensen, Washington Department of Pediatrics, University of Washington School of Medicine and Major Harry R. Clypool, Lt. Colonel George N. A. and Captain William R. L. R. USAF (MC) with their clinical management of this child and briefly with the authors.

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## INTELLECTUAL ADVENTURE IN MEDICINE

"If anyone deserves to be nominated as a pioneer special ist in gastroenterology Dr William Beaumont would head the list. But in any such discussion one must not overlook Alexis St Martin who likewise contributed to science by permitting the experiments—experiments which caused him some di comfort and mental anguish. That these experiments were not harmful is attested by the fact that St Martin lived to be 76 years of age. He married and reared a family and was a strong healthy man. When he returned to Quebec from Mackinaw for the second time in 1831 he made the trip in an open canoe via the Mississippi and Ohio Rivers, Lake Erie, Lake Ontario and the St Lawrence River. The family arrived in Montreal in June having traveled more than 2 000 miles. Moreover St Martin outlived Beaumont by 15 years. The story of Beaumont and St Martin has been told many times but it bears repeating because it illustrates what can be done when the spirit of inquiry is combined with the spirit of intellectual adventure in medicine."

—CHESTER S KEEFER, M D  
in *The American Journal of Gastroenterology*  
p 194 Feb 1958



# Porphyria Hepatica With Primarily Psychiatric Manifestations

JAMES M. BAILEY, L. T. C. I. MC, USA  
ROBERT B. CARBECK, CPT, MC, USA

**T**HIS case is presented as a reminder that a significant number of psychiatric conditions have an organic cause. The non-psychiatrist when confronted with severe psychiatric symptoms is apt to immediately assume that they are psychogenic and to promptly refer the patient to a psychiatrist. The less severe symptoms which usually are passed off as neurotic are so frequent and so commonly psychogenic that only a feeble attempt is made to rule out an organic cause. One such cause is acute intermittent porphyria. This condition certainly is not as rare as is generally believed, and must be kept in mind as the possible cause of psychiatric conditions of all severity. In Sweden where porphyria has attracted a great deal of attention among physicians, incidence of acute intermittent porphyria is 1.5/100,000.

A patient was sent to us with a diagnosis of schizophrenic reaction, paranoid type. Because the possibility of an organic cause was kept in mind, the diagnosis was readily made and proper management instituted.

## CASE REPORT

The first indication of major psychopathology in this 39-year-old white male occurred in the spring of 1956. This consisted of a paranoid delusion concerning his commanding officer and was so intense that he went to the Office of Special Investigations concerning it. The patient stated that following this everything went well for about one year. In April and May 1957 the patient smelled exhaust fumes when driving in his automobile and believed that his neighbor was trying to kill him. In mid-May he consumed three-fifths of whiskey over a four-day period and ate poorly during this time. During and following this period his paranoid delusions subsided and became more evanescent. He was seated and vomited once. On direct questioning he admitted that he had diffuse, meprobamate low-grade minimal pain during this period. On the day following this period he experienced auditory hallucinations and tremors and was seen by a physician who gave him sedatives.

His hallucinations disappeared, but he became even more anxious over the next eight days and was sure someone was going to kill him. He was then hospitalized for 17 days and stated he was in a fog the first five days. At the time it was thought the episode was caused by alcoholism. It was recommended the patient join Alcoholics Anonymous which he did.

The patient denied ingestion of any alcohol subsequent to his hospitalization in May 1957. He joined Alcoholics Anonymous and attended faithfully until December. He was given phenobarbital  $\frac{1}{4}$  grain four times a day for nervousness beginning in July 1957. In spite of this he had episodes of fairly severe anxiety. He stopped the medication for four days and stated he felt better during this period, but nevertheless resumed the medication.

In December he stopped going to Alcoholics Anonymous and developed paranoid ideas concerning the director of the local Alcoholics Anonymous chapter. On 31 January 1958 he became very anxious, developed a severe bilateral frontal headache and began crying while at work. He was sent to the dispensary where he was given promazine hydrochloride 25 mg tablets to be taken four times a day and sent home. The phenobarbital was discontinued at that time. While at home he became very anxious and was sure someone was trying to kill him. He developed crampy lower abdominal pain and cramping pain in all four extremities. On 8 February his sensorium became clouded and he remembered very little that happened from then to 10 February but he did remember seeing robots on his front lawn. According to other sources he became increasingly agitated during that period. He was seen by a physician on 10 February and was described as being acutely excited with visual and auditory hallucinations rambling wildly and verbalizing many paranoid delusions. The patient stated that the following day while in the hospital he noted weakness of the right ankle and pain in the distal part of the right leg. He was transferred to this hospital on 12 February with a diagnosis of paranoid schizophrenia chronic severe.

On direct questioning the patient remembered two other episodes of confusion and agitation plus crampy lower abdominal pain. The first occurred in 1927 following ingestion of home-brew. The second episode occurred when the patient had infectious hepatitis in 1950. The family history was incomplete and noncontributory.

On general examination the patient was extremely cooperative and anxious to please. He was oriented and his memory was intact. His affect was grossly normal and his thought-production and stream of thought were good. He revealed many paranoid delusions which were not fixed but changed readily and were concerned with the cause of his psychotic episode. He denied hallucinations since 11 February. The remainder of the physical examination was entirely within normal limits.

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## CASE REPORT

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by photosensitivity occurring late (adulthood). The second group is the acute intermittent type, into which this case presentation falls. This is the most common type of porphyria. The third is the mixed type in which photosensitivity occurs with intermittent abdominal or nervous manifestations or both. Latent porphyria hepatica in which chemical abnormalities are found in the absence of clinical manifestations, is being encountered with increasing frequency.

As the name implies, acute intermittent porphyria is characterized by individual attacks of varying lengths of time, and with varying periods of remission. The major manifestations fall into three categories: Abdominal, neurologic and psychiatric. The abdominal manifestations are pain which is usually diffuse, colicky, and severe constipation, which may be so severe as to mimic bowel obstruction and nausea and vomiting. Under neurologic manifestations we find peripheral neuropathy, characterized by pain and paresis, or actual flaccid paralysis. This is most common in the lower extremities and is not symmetrical. Paralysis of trunk muscles is much less common, but paralysis of the respiratory muscles is a fairly common cause of death in these patients. In more severe cases bulbar involvement may occur.<sup>2</sup> Most commonly, the psychiatric manifestations are irritability and anxiety. These coupled with the "atypical" abdominal complaint are usually interpreted as indicating emotional illness. The patient may then become psychotic, which seems to confirm this diagnosis. "Organic" signs are present, such as confusion and disorientation but additional symptoms may mask these and make the physician think of a schizophrenic process. Visual hallucinations when present, are of the type seen by "organic" patients, and may be accompanied by auditory hallucinations. Other manifestations such as temperature elevation, leukocytosis, tachycardia and hypertension are also occasionally seen, which also confuses the picture. The urine is classically described as port wine in color, either as voided or on standing. This color is greatly overemphasized and is not always present.

It has been shown by several workers that certain chemicals such as the barbiturates,<sup>3</sup> ethyl alcohol,<sup>4</sup> and sulfonamides may precipitate an attack. Porphyria hepatica is inherited as a Mendelian dominant and may be latent or manifested clinically as either the acute intermittent, cutanea tarda, or mixed type.<sup>5</sup>

Diagnosis depends on the suspicions of the clinician, based on the clinical manifestations. A good but simple laboratory procedure is to check the urine for porphobilinogen by the Watson-Schwartz test. A positive test is almost pathognomonic of porphyria. Porphobilinogen has been found in a few instances of Hodgkin's disease, carcinomatosis, systemic sporotrichosis, and hepatic cirrhosis without clinical manifestations of porphyria.<sup>6</sup>

Quantitative tests for coproporphyrin and uroporphyrin may be performed but such tests are not widely available

Treatment of the acute episode is solely supportive Paraldehyde or chloral hydrate may be prescribed for restlessness and opiates or synthetic analgesics such as Demerol Hydrochloride for pain Barbiturates ethyl alcohol and sulfonamides are contraindicated during the acute attack and at any other time Recently it has been found that with chlorpromazine hydrochloride therapy there is a disappearance of pain and nervous symptoms There was however no effect reported on established paralysis In our case it is very possible that the phenobarbital the patient took from July through January precipitated his recent attack

### SUMMARY

A case of porphyria hepatica acute intermittent type, with predominantly psychiatric manifestations, has been presented as a reminder that this and other organic conditions may occur in such a manner The clinical manifestations and treatment have been briefly discussed

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—REGINALD W LUXTON M D

R T COOKE M D

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## Diabetic Acidosis With Transient Renal Insufficiency

CHARLES E. SHIELDS *First Lieutenant MC USA*

**D**IABETIC ketosis may produce a hypotensive state which in turn can occasionally induce oliguria or anuria.<sup>1,2</sup> Reported cases have been characterized by laboratory evidence of acute renal insufficiency, *i. e.*, azotemia and hyperkalemia. Renal suppression may be so marked that hemodialysis is required.<sup>3</sup>

This case report is of interest in that transient oliguria occurred in a diabetic who had not experienced hypotension during recovery from a mild episode of ketosis, and in whom there was no evidence of exposure to nephrotoxic agents, but who did demonstrate electrocardiographic and biochemical evidence of hypokalemia. Restoration of normal urinary output followed electrolyte replacement.

## CASE REPORT

A 32 year-old woman para 3 gravida 4 who had been diagnosed 12 years previously as a diabetic was admitted to this hospital on 9 January 1958 after a 24 hour period of anorexia and intermittent nausea and vomiting. Following institution of insulin in 1946 progressive increase in dosage had been required and 60 units of neutral protamine Hagedorn insulin (NPH) had been administered daily since 1947. Three previous pregnancies had been associated with ketosis resulting in a stillborn infant in the second trimester of the first pregnancy. The younger of two surviving children is mentally retarded. The current pregnancy had been uneventful except for an alleged attempt to induce abortion with quinine three months before the present hospitalization.

Past history was significant in that the patient had been hospitalized for right upper lobe pulmonary tuberculosis in 1954. Following drug therapy she had been subjected to left resection from which she had recovered without incident. A parasternal series following retrosternal and subxiphoid pain had been reported as positive for hiatus hernia. There was no familial history of diabetes mellitus. The patient was normotensive.

From Vll y F r g Army H :it i t k o will i f j t Niall is n wa l g t  
t T pl r Army H :it i A f f A h e u f f i e f i t

Examination on admission revealed an acutely ill patient who was conscious and able to answer questions lucidly. Her blood pressure was 120/78 mm Hg, temperature 98.4 F, pulse rate 88 per minute, respirations 22 per minute and normal. Other than dryness of the mucous membranes there was no significant evidence of dehydration. Additional findings were the presence of scattered rales at both lung bases, uterine enlargement compatible with a six-month gestation, 1 plus pitting pretibial edema and essentially normal fundi. The remainder of the examination was unremarkable.

Routine urinalyses showed 3 plus albuminuria, 4 plus glycosuria and ketonuria. The reaction was acid with a specific gravity of 1.015. Microscopic examination of urinary sediment showed 6 to 8 white blood cells, occasional erythrocytes and granular casts per high powered field. Blood glucose was 193 mg per 100 ml, CO<sub>2</sub> combining power 17 mEq per liter, serum chlorides 103 mEq per liter, serum ketones were positive in a 1:12 dilution. Blood cell count revealed a leukocytosis of 16,700 per  $\mu$ l and a hemoglobin of 13.7 grams per 100 ml but was otherwise within normal limits. A cardiolipin microflocculation test was negative. A roentgenogram of the chest showed evidence of the right fifth rib and elevation of the right lateral of the diaphragm was noted without evidence of active pulmonary parenchymal disease. The electrocardiogram demonstrated changes consistent with hypokalemia (fig. 1). Other pertinent laboratory data are noted in table 1.

During the night of admission the patient had hematemesis, her blood pressure remained in a normotensive range. Urinary output was initially 60 to 80 ml per hour. Therapy during the first 12 hours consisted of penicillin given parenterally at a total of 150 units, fentanyl in 2 liters of 0.9 per cent sodium chloride solution and 2 liters of 5 per cent dextrose in water. Output during the same period was 720 ml of vomitus and 640 ml of urine. Although responsive the patient was uncooperative in taking fluids or medication orally.

The morning after admission the urinary output decreased to 5 to 10 ml per hour. Physical examination at that time revealed improvement of hydration as evidenced by moistness of the mucous membranes, good tissue turgor and moist axilla. However, an increase in bilateral rales and associated tachycardia of 130 to 140 resulted in the decision to digitalize the patient intravenously. Clinical improvement manifested decreasing pulmonary congestion and slowing of the pulse ensued. Oral digitalis maintenance was continued until the fifth hospital day.

Because of electrocardiographic evidence of hypokalemia and a serum potassium of 2.8 mEq per liter, it was elected to administer 60 mEq of potassium chloride by infusion despite the presence of urinary suppression. Combined output during a 31 hour period of oliguria was 990 ml (380 ml of urine and 610 ml of vomitus). Intake by parenteral and oral routes totaled 1,490 ml. Emesis gradually abated either spontaneously or partially in response to intravenous

administration of pyridoxine hydrochloride. At the expiration of 31 hours diuresis suddenly occurred with urinary output of 200 to 225 ml per hour.

Two urine cultures were positive for beta hemolytic streptococci and *Micrococcus pyogenes* var *albus* respectively. Toxicologic analyses of feces, urine and blood were negative. Antistreptolysin was 250 Todd units and the C reactive protein was negative.

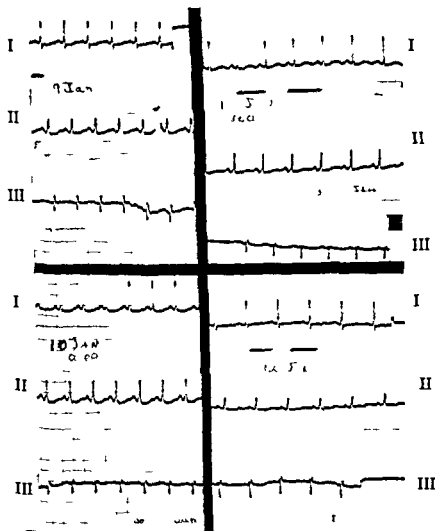


Figure 1 Electrocardiogram demonstrating changes consistent with hypokalemia.

Electrocardiograms obtained simultaneously with blood chemistry studies revealed hypokalemia (fig 1 and table 1). During this time there was no other significant electrolyte imbalance nor nitrogen retention. The electrocardiogram returned to normal paralleling biochemical improvement. Urinalyses demonstrated persistent albuminuria, pyuria, and cylindruria with occasional microhematuria. Urinary specific gravities ranged from 1.007 to 1.020.



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Once diuresis occurred the patient's course was uneventful except for a brief recurrence of ketonuria and ketonemia. Administration of regular insulin and augmentation of fluid intake produced amelioration. Five hundred milliliters of whole blood were administered because of a hemoglobin of 10.7 grams per 100 ml. Blood loss was thought secondary to a possible esophagitis. Urinary output was well maintained and oral intake rose to 2 liters daily. The patient was subsequently placed on an 1800 calorie diabetic diet. Interval insulin dosage was dictated by the degree of glycosuria or hyperglycemia. She was discharged to an outpatient status on a regimen of 35 units of NPH with 5 units of regular insulin in the morning and 5 units of NPH in the evening. The subsequent prenatal period was uneventful and the patient delivered a viable 8 pound baby girl on 9 March in the thirty-fifth week of pregnancy. In the immediate postpartum period diastolic blood pressures averaging 100 mm Hg were demonstrated.

*Comment.* Analysis of initial fluid replacement following admission of this patient would indicate that excessive amounts of sodium chloride were administered. There is a good possibility that hyperosmolarity was induced by excessive administration of sodium chloride. The delay in administration of potassium undoubtedly potentiated the pathophysiologic shift of this ion from the intracellular to the extracellular compartment and its subsequent diuresis. More liberal administration of water might have aborted the oliguric episode described in the case report.

### DISCUSSION

Historically, there was no evidence in this patient of hypotension, documented renal disease, toxemia of pregnancy, hemolysis or obstructive uropathy. Toxicologic investigation was negative. The sudden onset of oliguria initially suggested acute renal damage, but subsequent restoration of urinary concentrating ability and the absence of bacteremia and fever would tend to exclude such profound insults as necrotizing papillitis<sup>4</sup> or cortical necrosis.<sup>5,6</sup> Reflex anuria seemed unlikely because of the experimental documentation that such urinary suppression rarely exceeds 80 minutes.<sup>7</sup>

In replacement therapy for acidosis without concomitant administration of potassium there is an intracellular shift of sodium with displacement of the former ion.<sup>8</sup> Rahman and Cannon<sup>10,11</sup> and their associates question whether increased intracellular sodium may not impede re entry of potassium into the cell. Elkinton, Winkler and Danowski<sup>12</sup> demonstrated that only by the administration of exogenous potassium was there adequate repletion.

Inasmuch as potassium will favor sodium retention, chronic hypokalemia will lead to interference with tubular function in the conservation of electrolytes and water.<sup>9</sup> In the study of

chronic potassium deficiency induced by purgation Schwartz and Relman demonstrated that restoration of potassium to normal levels resulted in sodium retention Investigation of patients included in another study<sup>1</sup> revealed impaired glomerular and tubular function with decreased clearances and isosthenuria which ultimately responded to potassium replacement It has been the impression of other workers that renal concentrating ability was impaired only when hypotension was present They did concede however that hypokalemia could alter tubular function

Potassium deficiency is frequently associated with permanent histologic abnormalities involving the liver pancreas skeletal muscle myocardium and kidneys

Evaluation by standard electrophotometric technics may reveal normal depressed or elevated potassium values unrelated to the total body concentration of this ion<sup>1 26</sup> A diabetic in ketosis has diminution in extracellular volume with increased serum electrolyte concentration which does not accurately reflect total body concentration Studies utilizing radioactive potassium (potassium 42) have demonstrated that a loss of one third of the body's potassium may coexist with serum levels of 8 mEq per liter<sup>1</sup>

Moderate hypokalemia frequently occurs in the therapy of diabetic ketosis because of dilution and intracellular migration of that ion Balance studies have shown this relative deficiency and replacement therapy at the time of the observation has aided in the correction of acidosis and metabolic imbalance<sup>1</sup> Bland emphasized that potassium can be decreased intracellularly before electrocardiographic biochemical or clinical changes become manifest To demonstrate hypokalemia several hundred mEq must be lost

The apparent cause and effect relationship in the patient described would indicate that potassium imbalance was directly related to urinary suppression The absence of stigmata of acute renal failure post diuresis would imply that this chain of events was not in operation The presence of albuminuria and abnormal urinary sediment suggest that antecedent renal disease may have been present in this patient before the acute illness though these findings may be found and thereby possibly be part of the renal pathophysiology of potassium depletion

#### SUMMARY

A case of diabetic ketosis occurring in a 32 year old woman without known antecedent renal disease is presented During therapy a 31 hour period of oliguria occurred Diuresis and recovery followed the administration of potassium chloride It has been emphasized that transient renal insufficiency may

have had its inception secondary to the induced hypernatremia and concomitant hypokalemia. Various pathophysiologic and experimental data have been submitted to support this thesis.

**ACKNOWLEDGMENT** The author wishes to thank Major George B. Hamilton MC USA for his assistance in the preparation of this article.

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### REDUCTION OF AUTO PEDESTRIAN COLLISIONS

Further reduction auto p destr an coll s ons can c m o ly from a g neral r cognition and ccepta ce of th phys l circum t nces nvolv d Intens f d ed c tion al fforts must b m de to nl ght n pedestrians (and all drive re occ s o lly pedestrans) relat e to the phys l facts which c n spa them injury r death Pe de tr ans m st learn th t hicle re deadly h gh energy object They m st als learn that very vehicle n motion car i a collis n zone whch pand wth peed and sh uld th y ent such zone t the wrong time or dwell in on fo more th n a br ef nterval injury or death is almost rta regardl ss of the t ns of the dr v r They m t als rec g ize the visibil ty limitations of divers C r ma ufacturers h uld be en ouraged to p vide wind h ld of the hight possible lght t ans m tran e They sh ld lso cont bute to pedest n safety by red ci g th jury pore t l of external mament tio D ngerous on m r r n should be bol sh d by unif m traffic leg l t o The langu ge of ped trian right f w y laws should be cons d red having n mind that th l ws of phy s dom te ll coll s ons Fn lly the i t grated p t t m f the e coll s ns l d to e s mple concl n The o ly t m a p de tr an can fely erc e hi right of w y /t v h cl have str pped not befo

—WILLIAM W HARPER

A W d c

p 272 Ap 1958

# Pericarditis Preceding the Clinical Recognition of Pneumococcal Pneumonia

PERRY B MILLER *Major USAF (MC)*  
NEWTON D SCHERL *Captain USAF (MC)*

**P**NEUMOCOCCAL PERICARDITIS, a once dreaded complication of pneumococcal pneumonia, has become relatively rare since the advent of antibiotic therapy<sup>1-</sup> The quick response of pneumococcal pneumonia to penicillin and other antibiotics prevents the entrance of the organism to the pericardium, especially because the most common preceding event, the development of empyema with subsequent direct spread to the pericardium, is forestalled<sup>2</sup>

Levine<sup>2</sup> emphasized that pericarditis occurring with pneumonia is (1) not a common complication of pneumonia (2) occurs almost exclusively in those cases of pneumonia complicated by empyema, especially empyema of the left pleural cavity and (3) occurs most often late in the disease

In the following case an unusual sequence of events was observed in which, at a time when physical examination and a roentgenogram of the chest revealed normal pulmonary findings, a pericarditis was diagnosed by the presence of a pericardial friction rub and compatible electrocardiographic changes, only to be followed 24 hours later by the clinical demonstration of a pneumococcal pneumonia

The clinical course observed in this patient is being reported because no mention of the appearance of pericarditis before the development of pneumococcal pneumonia could be found in the standard textbooks of medicine, cardiology, and pathology consulted<sup>1-</sup>

## CASE REPORT

A 20-year-old man was admitted to this hospital on 5 March 1958 complaining of mild lower anterior chest pain aggravated by deep inspiration the pain had been present for twenty four hours. He had

experienced weak ss anorexia and nausea on the day of admission. There was no history of cough chills or known fever.

Physical examination on admission revealed no abnormalities except for a minimal temperature of 99.4 F.

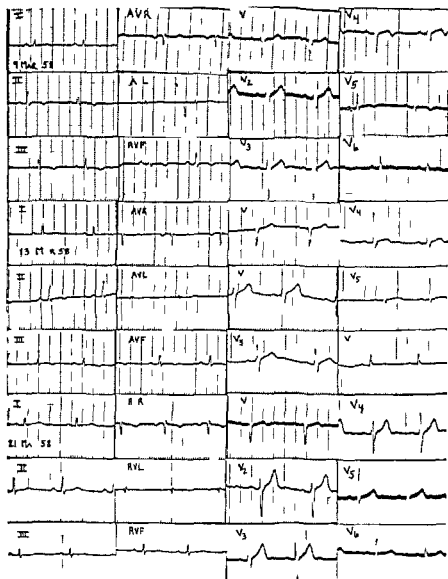


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1958 T b T u c h a n g a r l m k d a d l t u r t w d o r m a l  
21 M h 1958 N m l l t a d g a m

The initial white blood cell count showed 15 000 cells per  $\mu$ l with 92 per cent neutrophils. The hemoglobin was 13.4 grams per 100 ml. The urinalysis was negative. A roentgenogram of the chest was negative.

On 6 March the patient had a marked rise in temperature to 105°F. A complete physical examination again revealed no abnormalities. Several blood cultures drawn at this time were found subsequently to be negative.

On 7 March a faint pericardial friction rub was heard over the third intercostal space at the left parasternal line. This was best heard with the breath held midway in the respiratory cycle and could not be heard with either full inspiration or full expiration. An electrocardiogram revealed the presence of coved T wave inversions in leads II, III, aVF and leads V<sub>1</sub>, V<sub>4</sub>. The T wave was upright in lead aVR (fig. 1). Physical examination of the lungs again revealed no abnormalities and a repeat roentgenogram of the chest was negative. The patient had continued to complain only of slight anterior chest pain. His temperature graph showed a spiking course varying from 99.6° to 104.8°F.

On 8 March bronchial breath sounds were audible and pectoriloquy was present below the angle of the left scapula. A roentgenogram of the chest revealed pneumonia in the apex of the left lower lobe (fig. 2). A white blood cell count showed 26 750 cells per  $\mu$ l and the differential count revealed 92 per cent neutrophils. The patient was now coughing and a sputum culture revealed *Diplococcus pneumoniae*. At this time the pericardial friction rub was more prominent than on the preceding day and could be heard in all phases of respiration. Crystal line potassium penicillin G was given in a dosage of 180 mg (300 000 units) intramuscularly every 3 hours for 4 doses. Procaine penicillin G was given in a dosage of 600 mg (600 000 units) intramuscularly every 12 hours.

On the following day, 9 March, the patient's temperature fell with a maximum spike to 101.8°F. The pericardial friction rub was still audible.

On 10 March the friction rub could no longer be heard although electrocardiographic changes were still present. The patient became afebrile and asymptomatic on this day and remained so until discharged on 19 March. An electrocardiogram taken on 13 March revealed marked improvement with a return of the previous T wave inversions toward normal (fig. 1).

A roentgenogram of the chest on 17 March demonstrated complete resolution of the pneumonia. A normal electrocardiogram was obtained on 21 March, two days after discharge (fig. 1).





Fig 2 R ig m 8 Mar b 1958 l g p m  
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### DISCUSSION

This case presented the problem first of a fever of undetermined origin and then of a pericarditis of unknown cause until the development of a classical pneumococcal pneumonia gave the key to the cause and indicated therapy for the disease.

The fact that the friction rub when first discovered could be heard only in the mid phase of respiration would argue for the diagnosis of a pleuropericardial friction rub rather than a pericardial friction rub (and indeed a pleurisy likely was present) but at that time the findings of electrocardiographic changes compatible with a pericarditis and the subsequent development of a pericardial friction rub uninfluenced by respiration indicate that pericarditis was present. In all probability the infection first developed in a pulmonary focus adjacent to contiguous pleura and pericardium with subsequent spread to the pleura and then to the pericardium. Probably there was a delay in the

involvement of a greater area of lung which prevented the clinical and roentgenologic diagnosis of pneumonia until after the signs of pericarditis had become manifest.

Before the onset of the pneumonia, the principal diagnosis considered was acute benign pericarditis. Acute benign pericarditis may be accompanied by high fever, leukocytosis, and virus pneumonia.<sup>7</sup> The similarity of the clinical picture as seen in this case to that seen in some cases of acute benign pericarditis indicates the possibility of difficulty in the differential diagnosis of the two diseases.

Steroid therapy has been reported to cause amelioration of the clinical course of acute benign pericarditis.<sup>8-10</sup> This case illustrates the need for caution in the giving of steroid therapy too early in the course of what appears to be acute benign pericarditis, since the diagnosis may be in error and the steroid therapy contraindicated for the actual disease present.

#### SUMMARY

In a patient with pericarditis, of apparent pneumococcal etiology, the unusual clinical picture of pericarditis preceding the clinical recognition of pneumococcal pneumonia was observed. Penicillin therapy resulted in prompt subsidence of the pericarditis and resolution of the pneumonia. The similarity of the clinical findings to some cases of acute benign pericarditis is discussed.



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unsuccessful. The oropharynx was injected but no exudate or membrane had appeared. The lungs were normally resonant. The heart was not enlarged and had a regular rhythm without murmurs. Abdominal examination disclosed no abnormalities. Homans' sign was negative bilaterally.

Neurological examination findings were as follows: Cranial nerves I—not tested II—intact III IV VI—intact V—anesthesia to hot and cold of the right side of the face with left side of face normal findings reversed themselves 12 hours after admission VII—complete peripheral facial paralysis on the left no taste bilaterally on anterior tongue to alcohol VIII—nystagmus to the left plus vertical component patient fell to the left with subjective external vertigo to the right when standing audition normal IX—left palate hanging with poor gag reflex X XI XII—dysphagia protrusion of tongue to left intact sternal cleidomastoids head held to right voice deep and hoarse Cerebellar signs Positive Holmes' rebound phenomenon on left moderate finger to nose dysmetria on the left poor ankle to knee motions bilaterally adiadochokinesis on the left Sensory Hemihypesthesia with no hot or cold differentiation on the right below the clavicles Deep tendon reflexes were present with the right upper extremity hyperactive superficial reflexes were absent plantar responses were normal.

Hemoglobin was 14 grams per 100 ml Hematocrit was 43 per cent. The white blood cell count was 11,000 per  $\mu$ l with 80 per cent neutrophils 16 per cent lymphocytes 3 per cent monocytes and 1 per cent basophils. Urinalysis was normal. Cholesterol was 321 mg per 100 ml blood urea nitrogen 18 mg per 100 ml blood glucose 68 mg per 100 ml. Cerebrospinal fluid on the fifth hospital day was xanthochromic with 2,600 red blood cells per  $\mu$ l plus 5 lymphocytes per  $\mu$ l, Pandy's test was slightly positive total protein was 53 mg per 100 ml.

For the first 36 hours the patient's respirations were normal. A prophylactic tracheotomy was performed and a moderate amount of mucopurulent material was aspirated from the bronchi. Large amounts of penicillin and streptomycin sulfate were given morphine was administered every 6 to 8 hours anticoagulants were not used.

On 9 July the patient suddenly became cyanotic and completely flaccid after five hours in a respirator he was able to breathe adequately. Subsequently left chest motion ceased until bronchoscopy aspirated a large mucus plug. Several more cyanotic episodes occurred with death ensuing during the morning of 17 July.

#### Autopsy Findings

At autopsy the only significant finding besides bilateral pneumonia was in the brain. The brain weighed 1,275 grams. The cerebral hemispheres were symmetrical their gyri were not flattened and the sulci were of the usual width. The brain stem appeared flattened, with the medulla measuring 3.2 cm in width being flattened to the area of the pons. The whole medulla/pons area (see Fig. 1) was flattened on the lower surface of the left side of the brain (Fig. 2 and 3). In the

interior of the medulla oblongata massive hemorrhage involved nearly the entire left half paralyzing the lower extremities and the lateral reticulospinal tract further extended across the midline to compromise the contralateral medullary structures (fig 3) Additional blood was seen above the roof of the medulla in the region of the fourth ventricle

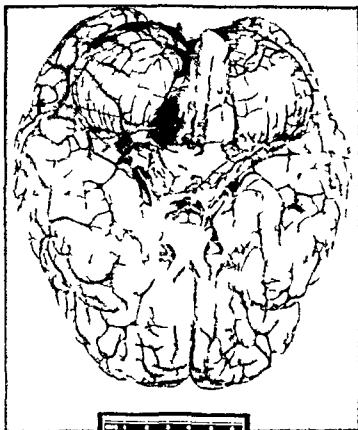


Figure 1 View of brain showing bulging of the left medullary

and also accumulated on the posterior cerebellar peduncle. The cervical spinal cord below and the brain stem above the involved medullary region were normal. Blood vessels at the base of the brain were structurally intact including the beginning parts of the posterior inferior cerebellar artery.

#### CLINICOPATHOLOGIC CORRELATION

Several aspects of this case deserve emphasis including the classic features of Wallenberg's syndrome. The initial complaint of sudden headache with vertigo is duplicated in other reported cases. Twenty seven of the 98 patients reported on by Lewis, Littman and Foley had an acute onset of sudden dizziness and headache. In the remaining patient these symptoms



Figure 2 Close up of figure 1

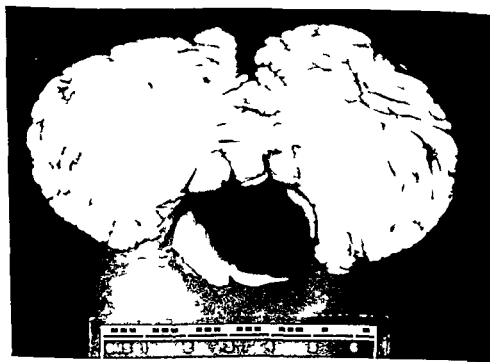


Figure 3 Correlation of brain specimen showing massive medullary hemorrhage and its relationship to the

# Coexisting Ovalocytosis and Hemoglobin C Trait

EDWARD S. MONGAN, Cpt MC USA

**O**VALOCYTOSIS is an abnormality of erythrocyte morphology in which the cells are oval or elliptic. It is a hereditary trait transmitted by either sex as a Mendelian dominant. Although its exact incidence is unknown, it is relatively uncommon. There are no known racial or sexual predispositions. Usually ovalocytosis does not produce ill health or anemia, but in about 12 per cent of the cases mild hemolytic phenomena can be found.

Hemoglobin C was first described in 1950 by Itano and Neel. It is an inherited abnormality of human hemoglobin detected by electrophoretic studies. The trait is usually asymptomatic, yet hemolysis and mild clinical symptoms can be found in patients with homozygous hemoglobin C. Cases of hemoglobin C trait have been described in association with other abnormal hemoglobins, notably with hemoglobin S.

In 1956 Avery reported two children who had ovalocytosis and hemoglobin C trait. In her cases the two hereditary abnormalities did not produce a summation of effect; for neither child had any evidence of an increased hemolytic process. The following is a case report of another patient with coexisting ovalocytosis and hemoglobin C trait.

## CASE REPORT

The patient, a 25-year-old Negro, was first admitted to this hospital on 24 January 1957 with a chief complaint of cough of one week duration. The cough was productive of one-half cupful of whitish sputum daily. About six months before his admission he noted the onset of nervousness, weight loss, decreased heat tolerance, and a weight loss of about 10 pounds despite good appetite. On the day of admission he developed chill, fever, and right-sided chest pain.

There was no family history of tuberculosis, diabetes, allergy, anemia, or of any hematologic disorder. Both parents, four brothers, and two sisters were alive and healthy.

From William B. Mum, Army Hospital, El Paso, Texas; David M. G. W. T. H. U. ty f R ch, M d a l C t 260 Cr d B l d R h N Y

Physical examination revealed an acutely ill well developed man. His blood pressure was 140/70 mm Hg pulse rate 120 beats per minute temperature 104.2°F and his respiratory rate was 32 per minute. His skin was hot moist and rather fine. There was bilateral exophthalmos but no diplopia. The thyroid was diffusely enlarged—about three times the normal size. There were decreased breath sounds and a few moist rales at both bases posteriorly. The remainder of the physical examination was within normal limits.

Laboratory data on admission included a white blood cell count of 24,100 per  $\mu$ l with 89 per cent neutrophils, 8 per cent lymphocytes and 3 per cent monocytes. Hemoglobin was 14.7 grams per 100 ml and the hematocrit was 42 ml per 100 ml. Urinalysis, serologic tests for syphilis, throat culture and three sputum cultures for bacterial pathogens, fungi and tuberculosis were normal. A tuberculin skin test using second strength PPD was positive. Histoplasmin and coccidioidin skin tests with a dilution of 1:100 were negative. A roentgenogram of the chest revealed a bilateral basilar pneumonitis. Total serum cholesterol was 120 mg per 100 ml, protein bound iodine was 17.9  $\mu$ g per 100 ml and basal metabolic rates after the pneumonitis had cleared were plus 32 and plus 39 per cent. By the second hospital week the white blood cell count was 5,500 per  $\mu$ l with 60 per cent lymphocytes. The lymphocytosis persisted for the rest of the hospitalization. On all blood smears there was from 40 to 60 per cent ovalocytosis and some anisocytosis (fig. 1). The red blood cells on occasion appeared hypochromic. Paper electrophoretic studies of the patient's hemoglobin revealed CA hemoglobin. A sickle cell preparation was negative. The patient's hemoglobin and hematocrit were within normal limits at all times.

The pneumonitis responded promptly on bed rest and penicillin therapy. A repeat roentgenogram on 31 January showed resolution of the pneumonia. After the diagnosis of hyperthyroidism was established the patient was started on Tapazole (brand of methimazole) on 12 February. By 25 April his basal metabolic rate was normal and he clinically appeared euthyroid. He was then started on Lugol's solution without any noticeable diminution in the size of the thyroid gland. On 16 May a subtotal thyroidectomy was performed which the patient tolerated well. His postoperative course was uneventful and except for the exophthalmos which persisted he remained euthyroid. He was returned to duty on 25 May and arrangements were made to follow him in the ophthalmology clinic.

The patient was readmitted to this hospital on 26 August with a 10-day history of cough. For a week prior to admission he had no cough, night sweats, chills, nausea and anorexia. On the day of admission he developed some right anterior chest pain which was made worse by inspiration. In the month prior to admission he had lost 16 lbs.

Physical examination revealed an acutely ill young man. Temperature was 101°F, pulse 96 beats per minute, respiration 20 per minute and his blood pressure was 120/62 mm Hg. There was no



## Coexisting C Hemoglo

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F m William B um r Army l  
U ty f R ch t N dic l c

September 1958)

# CASE REPORTS—OVALOCYTOSIS AND SICKLE CELL TRAIT 1977

concentration was 34 per cent. Red blood cell fragility showed an increase in hemolysis in both the control and in the patient. A concentration of 0.48 per cent NaCl with complete hemolysis in the control and 0.28 per cent in the patient. The direct bilirubin was 0.16

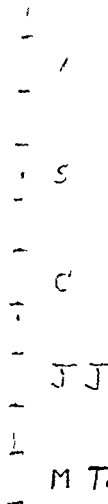


Figure 2 Photograph of the filter paper on which the electrophoretic studies were made. "S" represents normal adult hemoglobin. "S" represents homozygous sickle cell hemoglobin. "C" represents homozygous C hemoglobin. "JJ" represents normal adult hemoglobin in a patient with ovalocytosis and "MT" represents the hemoglobin of the patient in this report. Note that he has CA hemoglobin.

mg per 100 ml and the indirect bilirubin was 0.52 mg per 100 ml. The serum uric acid was 0.25 Ehrlich units per two hours. The serum cholesterol was 195 mg per 100 ml, the protein bound iodine was 7.9 and 6.4 µg per 100 ml, and the basal metabolic rate was minus 16 and minus 4 per cent. Blood culture and serologic tests for syphilis were negative on admission. Six gastric washings were negative by culture for fungi and tuberculosis. Tuberculin and coccidioidin skin tests were

positive the histoplasmin skin test remained negative. The white blood cell count returned to normal two weeks after admission and remained so. There was never an eosinophilia. The patient was not anemic throughout his second hospitalization. The admission roentgenogram of the chest showed a pneumonitis at the right base and some right hilar adenopathy. These roentgenographic findings did not clear completely until November. The electrocardiographic findings were within normal limits.

The patient was placed on bed rest and penicillin but his symptoms did not clear promptly and his rightsided chest pain persisted. On the sixth hospital day treatment was given without benefit. The antibiotics were discontinued after two weeks. A tentative diagnosis of pulmonary coccidioidomycosis was made on the basis of the clinical picture, the hilar adenopathy, the lack of response to antibiotics and the conversion of the coccidioidin titer between January and August 1957. The patient continued to run a low grade fever for the first month of hospitalization but was afebrile thereafter. Complement fixation test for coccidioidomycosis was positive 1:4 on 11 September and by 2 December was positive to a dilution of 1:128. On this basis dissemination of the fungus infection was postulated although the patient continued to have no clinical evidence of dissemination. The patient was treated supportively in the hospital until the complement fixation test for coccidioidomycosis started to decrease in January 1958 to 1:64 and then stabilized. Throughout his hospitalization the patient was closely followed in the ophthalmology department for his exophthalmos. He was given a month trial of Serpasil (brand of reserpine) without any effect on the exophthalmos. He was started on thyroid extract to toleration for the same reason. At the time of discharge he was on 390 mg of thyroid daily without much improvement. He returned to duty on 27 March and is being followed in the ophthalmology and chest clinics.

#### COMMENTS

The presence of over 40 per cent ovalocytosis on all the blood smears completed on this patient during his two hospitalizations established the diagnosis of ovalocytosis. The electrophoretic studies of the hemoglobin on two occasions confirmed the diagnosis of hemoglobin C trait. There was no clinical or laboratory evidence of increased red blood cell destruction in this patient. Unfortunately it was impossible to study his family. Despite the presence of a bilateral pneumonia, thyrotoxicosis and disseminated coccidioidomycosis in a 14 month period the erythrocyte abnormalities in this patient at no time were clinically evident. His recovery from all three illnesses occurred as promptly as could be expected. This finding is in keeping with the conclusion of Avery that these two abnormalities do not produce a summation of effect. Since increased hemolysis does occasionally occur in either of these two conditions in the heterozygous state one would expect a small percentage of patients with both

abnormalities to show some evidence of increased erythrocyte destruction. If one of the conditions were homozygous, moreover, increased hemolysis would then probably be expected.

### SUMMARY

A case of coexisting ovalocytosis and hemoglobin C trait is reported. There was no laboratory or clinical evidence of increased red blood cell destruction. These two abnormalities evidently can be associated without a summation of effect.

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### HOW TO USE A PLACEBO

The question of whether a placebo is a physical or a psychologic form of treatment has caused much confusion. The answer seems to be that it is a psychologic form of treatment employing a physical substance. The moral problem of honesty that has clouded the issue and has often resulted in hedging and self-deception on the physician's part could be avoided if a psychologic frame of reference were explicitly acknowledged and used. This requires however that the physician be able to view psychotherapy as a legitimate and effective therapeutic measure. The selection of patients for treatment with a placebo should be based on the usual criteria for the selection of one or another psychologic technic. Since the placebo aims at the eradication of symptoms it should not be employed when an etiologically oriented therapeutic approach is feasible.

—MARCH HOLLENDER M D  
n *American Psychiatric Association Digest of Treatment*  
p 217 Feb 1958

## Departments

### GEN HARRY G ARMSTRONG LEADER IN AVIATION AND SPACE MEDICINE RETIRES

Major General Harry G. Armstrong, USAF (MC), a pioneer in aviation and space medicine and former Surgeon General of the United States Air Force, retired 1 September after almost 30 years military service.

A rare combination of research and clinical physician and military administrator, General Armstrong was the first to conduct many experiments which provided the medical knowledge that enabled man to fly at the great altitudes and high speeds of today's aircraft. On 9 February 1949 while he was Commandant of the U.S. Air Force School of Aviation Medicine, he established the Department of Space Medicine—the first laboratory of its kind. He is the author of *Principles and Practice of Aviation Medicine* which is now widely used throughout the world as the standard textbook in this specialty. He is also the author of more than 75 scientific papers on aviation and space medicine.



General Armstrong

In 1934 Major General Malcolm C. Grow and General Armstrong founded the Aero Medical Laboratory at Wright Patterson Air Force Base, Ohio, and General Armstrong was selected as the first Director.

In 1936 General Armstrong won the Williamson Award of the Association of Military Surgeons, and in 1940 he was a co-recipient of the Collie Trophy given annually for the greatest contribution to aviation. In 1941 he received the John J. Jeffries Award from the Institute of Aeronautical Sciences. The Aeronautical Medical Association in 1949 honored him with the Theodore C. Lyster Award for eminence in aviation medicine.

General Armstrong served as president of the Aero Medical Association and the Association of Military Surgeons in 1952—the first person to head both of the societies simultaneously. For the past three years General Armstrong has been serving as Surgeon of the United States Air Force in Europe. During this period he organized a Central Aero Medical Group which renders special operational aeromedical support to the USAF Command and to NATO nations. He was actively promoting inter-national conferences with European countries in the French Branch of the Aero Medical Association and in fostering development of an all-European Branch of the Aero Medical Association. In 1956 he organized the first German-American Joint Aviation Medicine Symposium where outstanding scientists in aeromedical research exchanged information.

## FOUR NAVAL MEDICAL AND DENTAL OFFICERS SELECTED FOR PROMOTION TO REAR ADMIRAL



*Capt Chrisman*



*Capt Galloway*



*Capt Kreuz*



*Capt Schantz*

Four captains of the Medical Department of the Navy Allan S Chrisman Calvin B Galloway Frank P Kreuz Jr Medical Corps and Curtiss W Schantz Dental Corps were recently selected for promotion to Rear Admiral Captain Chrisman is the Commanding Officer U S Naval Hospital San Diego Calif Captains Kreuz Galloway and Schantz are at the National Naval Medical Center Bethesda Md commanding the U S Naval Hospital U S Naval Medical School and U S Naval Dental School respectively

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## A M A SECTION ON MILITARY MEDICINE ELECTS DR ALPHONSE McMAHON CHAIRMAN

Alphonse McMahon M D Associate Professor of Medicine St Louis University School of Medicine and Rear Admiral MC USNR (Ret ) was elected Chairman of the Section of Military Medicine of the American Medical Association at the annual meeting in San Francisco in June George H Houck M D Palo Alto Calif was chosen Vice Chairman Other officers included Colonel Charles H Bramlitt USAF (MC) Washington D C Charles L Leedham M D Cleveland Ohio who were elected Secretary and Delegate respectively Captain Robert V Schultz MC USN Washington D C was named Representative to the Scientific Exhibit



*D McMahon*

# GEN PAUL ROBINSON RETIRES SUCCEEDED AS MEDICARE CHIEF BY COL WERGELAND

Major General Paul I. Robinson MC USA Executive Director of the  
Dependent Medical Crep g m since its inception in December  
1956 will become coordinator for medical relations for the Metropolitan  
Life Insurance Company when he retires 31 August after more than  
30 years active service. General Robinson will be succeeded by  
Colonel Floyd L. Wergeland MC USA now Assistant to the Executive  
Director.



Gen Robinson



Gen Schwichtenberg



Gen Seeley



Gen Mattingly

Three other medical officers whose retirement have been  
announced are Brigadier General Albert Schwichtenberg USAF (MC)  
formerly Surgeon of the Air Defense Command Brigadier General Sam  
F. Seeley MC USA Chief of the Professional Division of the Office  
of the Army Surgeon General Washington D C and Brigadier General  
Thomas W. Mattingly MC USA Chief of the Department of Medicine  
Walter Reed Army Hospital General Schwichtenberg has been ap-  
pointed Head of the Department of Aviation and Space Medicine of  
the Los Angeles Foundation Albuquerque New Mexico General Mattingly  
who has served as one of the President's physicians will become  
Director of Medical Education at the Washington Health Center  
Washington D C On 1 September General Seeley will become a  
Professor of Anatomy of the National Research Council in Wash-  
ington D C.

## Official Decorations

The following awards were recently announced by the Depart-  
ment of the Air Force:

### Legion of Merit

Major General William Col USAF (MC) Albert H. Schwichtenberg Brigadier General G USAF (MC)

### Air Force Commendation Medal

Major General P. W. Dumas Col USAF (MC) Captain W. Bryant Col USAF (MSC)

# OFFICERS CERTIFIED BY SPECIALTY BOARDS

## Supplementary Listing

The Surgeons General of the military medical services have announced that the following regular Medical and Dental Corps officers have been certified by the boards indicated since the listings published in previous issues of the *Journal*

### American Board of Pediatrics

Thomas A. H. Capt. USA      Edward C. M. Ke. Capt. USA

### American Board of Radiology

P. I. E. S. b. rt. Capt. USA

### American Board of Obstetrics and Gynecology

R. b. t. L. B. k. Lt. Comdr. USN	Er. s. F. L. tham, Lt. Comdr. USN
R. b. rt. K. Bart. Lt. Comdr. USN	W. l. r. M. L. rg. Lt. Comdr. USN
D. d. C. B. er. Lt. C. mdr. USN	K. a. th. N. M. M. f. USAF
W. R. B. yd. Comd. USN	D. ld. J. Summ. so. Lt. C. l. USA
G. org. A. B. r. na. Lt. Comd. USN	G. rge. J. T. yl. Comdr. USN
Ch. l. E. G. bb. Maj. USAF	W. l. D. Tuck. C. pt. USN

### American Board of Internal Medicine

J. s. ph. T. H. g. Lt. USN	J. m. C. Sy. Maj. USA
W. ll. S. My. Lt. C. md. USN	H. rry. A. W. Cap. USN
H. ary. A. Spark. Lt. Comdr. USN	

### American Board of Pathology

#### *Pathologic Anatomy and Clinical Pathology*

R. h. d. B. Ar. k. ur. M. j. USA	Harry F. Sp. r. Lt. C. l. USA
P. t. B. M. c. mb. Cap. USA	

### American Board of Surgery

N. ma. J. C. l. M. j. USA	Har. ld. P. Par. Comdr. USN
J. s. ph. L. H. no. Maj. USA	W. lt. E. Sw. tz. r. Maj. USA
W. llam. T. L. b. rry. J. C. mdr. USN	M. J. Trumm. r. Lt. Comdr. USN

### American Board of Physical Medicine and Rehabilitation

R. b. rt. A. Gr. gg. Maj. USA

### American Board of Preventive Medicine

#### *Public Health*

H. rry. J. D. lly. Maj. USA	Charl. s. W. Ar. a. l. Lt. Col. USA
J. t. m. H. G. b. g. Capt. USA	

### Aviation Medicine

Cl. ud. M. Mea. C. l. USAF	Ch. t. ph. C. Shaw. Capt. USN
J. h. A. N. rt. Col. USAF	Alf. d. R. Stump. Jr. M. j. USAF
Ph. l. p. P. Pea. Col. USAF	Charl. A. V. t. h. Lt. Col. USAF
R. bert. k. Quin. ll. L. C. l. USAF	



*Occupational Medicine*

HILL D D E C P USAF

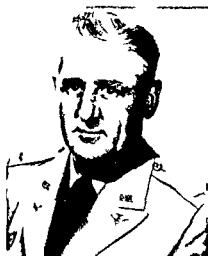
Chil W K I L C I USA

## American Board of Oral Surgery

K mbl A T g Comdr USN

## COL BERNIER NAMED OUTSTANDING DENTIST

Colonel Joseph L. Bernier DC USA has been included among the Twelve outstanding dentists of the United States in a permanent photographic exhibit in the University of Haiti Dental School Port au Prince Haiti. The selection made by the National Library of Medicine cites Colonel Bernier for his outstanding contribution to and development of the specialty of oral pathology. His present duty assignment is Chief of the Dental and Oral Pathology Section of the Armed Forces Institute of Pathology.



Col J L Bernier

In addition to Colonel Bernier the group includes John Greenwood (1760-1819) Horace H. Hayde (1769-1844) Solyman Brown (1790-1876) Eleazar Parmenter (1797-1874) Chapman Aaron Harris (1806-1860) Horace Well (1815-1848) Greene Verdmann Black (1836-1915) Henry Teddy Dean (1893) Kenneth A. Elsick (1893) William J. Gies (1872-1956) and J. Ben Robson (1883).

## SYMPOSIUMS ON MEDICAL ASPECTS OF ATOMIC WEAPONS

Armed Forces Special Weapons Project Medical Symposia are scheduled to be conducted at Santa Base New Mexico on 6-10 October 1958, 3-7 November 1958, and 16-20 March 1959. The symposia designed to orient medical personnel in the problem of detection, identification, clear weapon, the industrial and toxicological hazard of modern nuclear weapons and related subjects.

Applications to attend the courses should be submitted to the Surgeon General U.S. Army, U.S. Air Force or Chief Bureau of Medicine and Surgery U.S. Navy through channels.

## A MESSAGE FROM THE A M A

A Report on the Medical Use of Hypnosis, submitted by the American Medical Association's Council on Mental Health, was approved by the House of Delegates of the Association at the 107th Annual Meeting of the Association in San Francisco in June 1958. The experiences of World War II having contributed to a reawakened interest in hypnosis, a summary of the Report may be of interest to physicians serving in the military forces.

The work of the Council on Mental Health was limited to the specific theme of the medical use of hypnosis in its therapeutic aspects, because this seemed to be the most relevant area for consideration.

There was unanimous agreement that there was no need at this time to question the validity of the various phenomena elicited by hypnotic techniques. Actually, in the literature on hypnosis practically all of these phenomena have been noted in one way or another since the time of Mesmer. In spite of this, however, it is still difficult to arrive at a formulation of hypnosis that is completely satisfactory. The Subcommittee of the British Medical Association presented the following definition, with which there was agreement in general:

A temporary condition of altered attention in the subject which may be induced by another person and in which a variety of phenomena may appear spontaneously or in response to verbal or other stimuli. These phenomena include alterations in consciousness and memory, increased susceptibility to suggestion and the production in the subject of responses and ideas unfamiliar to him in his usual state of mind. Further phenomena such as anesthesia, paralysis and the rigidity of muscles and vasomotor changes can be produced and removed in the hypnotic state.

The Council emphasized certain regressive aspects of hypnosis. It also stressed the fact that hypnotic phenomena were of a wide variety and should not be limited only to the so-called trance state.

In order to begin to understand these phenomena, it is necessary to place hypnosis within the general framework of psychodynamic psychology and psychiatry. This has implications not only for the theoretical understanding of hypnosis, but also for its therapeutic application and will therefore be related in an important way to any teaching and training program. In a sense, it is unfortunate that the induction of hypnosis is generally so simple a matter that it requires little or no technical skill or training. This in itself, represents one of the main hazards in

From the Council on Mental Health of the American Medical Association.  
was developed by the early years of the Department of Psychiatry.  
—Ed to

*Occupational Medicine*

Hill d D E C p USAF

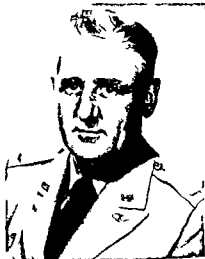
Charl W K ul L C I USA

## American Board of Oral Surgery

K mbl A T g Comdr USN

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C I I B

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## SYMPOSIUMS ON MEDICAL ASPECTS OF ATOMIC WEAPONS

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Applications and theses should be submitted to the Surgeons General U S Army or U S A Force to Chief Bureau of Medicine and Surgery U S Navy through the

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To the Editor —  
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Dr Samuel Bard  
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The Journal welcomes  
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1957 —Editor

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BLODGETT George Francis  
assigned to U S Naval  
from the University of  
appointed a lieutenant  
1930 died 9 July 1958  
of myocardial infarction

LOVE Jack Pratt Lieutenant  
assigned to the Office of  
Washington D C gradu  
Chicago Ill served in an  
December 1941 commiss  
United States 24 December  
Army 5 July 1946  
current address

## Reviews of Recent Books

PROGRESS IN ARTHRITIS edited by *J. H. Talbot* M.D. and *L. Maxwell* L.K. M.D. 456 pages illustrated by *Gund* Stitt I.N.W. Y.K.N.Y. 1958 P \$12.50

This is a convenient easy-to-read 456 page volume edited by well recognized authors and contributed to by a large number of other physicians many of whom are eminent in rheumatology. There are 64 pages covering the many facets of humeroidthritis. The other clinical entities in rheumatology are adequately discussed and illustrated and references are listed at the end of each chapter. Therapy is discussed in an analytical manner incorporating current pharmacological thinking. A very practical but hectic chapter on rehabilitation is timely and practical.

This volume will be found worthwhile to the internist rheumatologist teacher and student —FRANCIS W. PRUITT C.L.M.C. USA

PATHOLOGY FOR THE PHYSICIAN by *William Byrd* M.D. Dpl. Psych. M.R.C.P. (Ed.) H.F.R.C.P. (Ed.) F.R.C.P. (Lond.) F.R.C.S. (C) F.R.S. (Can.) LL.D. (S.K.) (Q.) D.S. (Man.) M.D. (O.I.) 6th edition thoroughly revised 900 pages 489 illustrations 12 plates 1 L. & F.B.G. Philadelphia P. 1958 P \$17.50

This sixth edition is a complete revision of Dr. Boyd's universally popular text of the pathology of internal diseases. The contents are arranged as to cover the various anatomic systems. 19 separate chapters and a final one on our internal environment. This latter includes coordination of the physiology and pathology of water, electrolytes and acid-base balances. The value of the book is enhanced by the easy-to-read writing style of the author. The various pathologic changes are explained by the correlation with the clinical signs and symptoms that they produce. The chapters devoted to the endocrine system are as up-to-date as is possible in a textbook and present this complex subject of endocrinopathology in a clear and understandable fashion. The chapter on the respiratory system contains

extremely interesting discussion of the relationship of smoking to carcinoma of the lung and typifies the excellent editorial style of this book. As the author states in the preface the text has been prepared with the graduate rather than the undergraduate student in mind, the physician or internist rather than the pathologist, the young rather than the old. This book is must in every physician's library.

—FRANK M. TOWNSEND C.I. USAF (MC)

ESSENTIALS OF GYNECOLOGY by *E. Stewart Tyler* M.D. 502 pages 343 illustrations 4 plates 1 L. & F.B.G. Philadelphia P. 1958 P \$12

This book fortunately lives up to its title. It is concise up to date, well organized and well written. The subject matter is adequately covered without verbosity and yet with enough detail to make it intelligible. The book is popular and practically illustrated.

The author has eliminated all controversial and archaic material and has set down a clear exposition of the subject as he sees it. Surgical indications and techniques are apparently those which he uses and approves. The book has evidently grown out of lecture material and as such is ideally suited for a text which can be amplified by lectures and discussions. It is also a ready reference.

The paper, typography, and binding are excellent. The index and bibliography are adequate. —ROY E. CROWDER, Capt, MC, USN

THE ACUTE ABDOMEN by William R. Quarth, M.D. Foreword by Warren H. Cole, M.D. 2d edition. 313 pages, illustrated. The Year Book Publishers, Inc., Chicago, Ill., 1958. Price \$6.50.

This compact volume deals with the acute abdomen from the viewpoint of differential diagnosis. It stresses the importance of emergency surgery in certain conditions, even though a definitive diagnosis is in doubt, and of equal importance, the contraindication of emergency surgery in other acute abdominal conditions. Arachnidism, periaarteritis nodosa, and pancreatitis are among the medical conditions for which the author considers operation contraindicated or harmful.

There is room for controversy concerning diseases for which operation can be delayed, and it is to the credit of the author that he mentions the differences of opinion. An example of this is the discussion on the treatment of acute cholecystitis. Chapter 3, Acute Intestinal Obstruction, has much worthwhile material in it and is probably the best chapter in the book.

The references listed at the end of each chapter are adequate to guide the reader to additional literature. This book is recommended for interns and residents in general surgery.

—PHILIP J. McNAMARA, Capt, MC, USN

AUSCULTATION OF THE HEART by Abe Rav, M.D. 166 pages, illustrated. The Year Book Publishers, Inc., Chicago, Ill., 1958. Price \$6.

A short but clearly and precisely written treatise on auscultation of the heart. This text should be extremely useful to the medical student as well as to the practicing physician who desires to get the most out of clinical examination of his patient. The author gives adequate importance to the study and evaluation of the heart sounds as well as murmurs. The descriptive material is adequately supported by sound tracings and by a uniform graphic system of recording auscultatory findings which make it easy for the reader to follow the text. A selected bibliography and index is provided.

—THOMAS W. MATTINGLY, Brig. Gen., MC, USA

CLINICAL ENZYMOLOGY edited by C. S. J. Martin, Sc.D. 241 pages, illustrated. Little Brown and Company, Boston, Mass., 1958. Price \$8.

This book is interesting to read not so much for the clinical applications which are limited but because it affords a glance at the present

complex ties of biological processes of which the enzymes are an essential part

Early clinical trials of enzymes were equivocal because of the difficulties of purification. Trypsin has had the most use and always seems to promise more than it actually gives. Streptokinase and hyaluronidase are still useful. Cholinesterase has many interesting facets but little clinical use. Parenteral use of enzymes is discussed. The small doses used are explained by the nature of enzyme action as catalyst. Examples of trypsin's effectiveness in treating acute thrombophlebitis are given. The basic action seems to be an anti-inflammatory effect. Interesting but inconstant effects have been noted in cancer in which at times there was arrest or shrinkage of the growth, relief of pain. The best results with little side reaction are obtained when trypsin is administered intramuscularly. Even then it must be taken to avoid getting the enzyme in the subcutaneous tissues. The chief complications usually pain and induration at site of injection. In the diagnostic use of enzyme, amylase determination is useful in acute pancreatitis, less so in chronic pancreatitis. Trypsinminase is of help in myocardial infarction. No mention is made of its use in infectious hepatitis. —JAMES L. TOBIN, C. L. USAF (MC)

ATRIAL ARRHYTHMIAS, DIGITALIS AND POTASSIUM by B. D. L. W. M. D., D. H. Rold, D. Lev. M. D. 222 pages. Illustrations. D. L. D. beger, M. D., I. B. K. I. N. W. Y. R. N. Y. 1958. P. \$6.90.

The authors present the thesis that atrial disorders during digital medication are frequent and are becoming more common in recent years. The material presented is based on both prolonged clinical studies and experimental experiments. The whole book is devoted to a detailed analysis of experimental and clinical evaluation.

The authors point out that the electrolyte balance of disordered heart beat may result from digitalis toxicity. They note that the individual with normal heart can tolerate large doses of digitalis but that with increased failure the rate between therapeutic and toxic dose narrows. It is emphasized that the lowering of body potassium concentration is an important factor in digitalis toxicity. Such hypokalemia occurs readily during modern therapy for cardiac decompensation. Much emphasis is placed on the importance of body electrolyte changes during heart failure and therapy therefor. The authors include numerous studies made on patients during hemodialysis both with and without associated digitalis therapy. Clinical studies are presented in detail including case summaries and individual comment on each case.

The book dwells largely on the electrocardiographic diagnosis of cardiac arrhythmia. There is also a chapter on the therapy of digitalis toxicity and 43 pages are all carried to speculation and hypothesis as to the action of digitalis in producing cardiac arrhythmias.

This book is written in excellent style and readily attracts and holds the interest of the reader. Opinions are stated objectively and with supportive data. The bibliography was well selected and

includes 198 references. Numerous clearly reproduced electrocardiograms illustrate the clinical and experimental data. The material is well presented from a scientific standpoint and accomplishes the stated purpose of the author. The book is principally of interest to students of internal medicine, cardiology, pediatrics, and physiology.

—BYRONA NICHOL Col MC USA

**PEDIATRIC CLINICS OF NORTH AMERICA** May 1958 Symposium on recent clinical advances. Alan Ross M D Consulting Editor. 558 pages. Illustrated. W B Saunders Company Philadelphia Pa. 1958. Price \$15 per year of four books issued quarterly (February, May, August, November). Sold only on a yearly basis.

This issue of the *Pediatric Clinics of North America* proves that the editors have used the title in its truest sense, because the entire issue is devoted to a symposium on recent clinical advances from Canadian authors. The caliber and scope of the articles further show that the level of Canadian pediatric practice is of the highest order.

Nineteen articles in this issue cover a wide field of pediatric practice, and a few are encyclopedic, while others highlight the more recent developments. The reader interested in the care of children will find most of the papers in this symposium of distinct practical value.

Of special interest to the practicing pediatrician are the chapters describing the newer laboratory procedures and their application to the investigation of pediatric disorders, the diagnosis and management of sex anomalies, and the diagnosis and management of the various types of rickets.

Several articles dealing with subjects currently much discussed in the lay press are included. These include an excellent guide to genetic counseling in some pediatric diseases, and two helpful chapters to aid the physician in his role of adviser when asked about reading disabilities and adoption. —THOMAS E CONE J Capt MC USN

**ON THE UTILITY OF MEDICAL HISTORY** Monograph I. Institute on Social and Historical Medicine. The New York Academy of Medicine. Iago Galdston M D Editor. 73 pages. International Universities Press. New York, N Y. 1957. Price \$2.

Organized to enquire whether medical history can serve to illuminate current problems and issues in medicine, the Institute on Social and Historical Medicine has now published the first of a series of monographs devoted to its proceedings. The present volume contains six interesting and highly readable papers which explore the topic. On the utility of medical history. The central concern is for the future of medicine.

The authors are eminent in either the field of medical history or in related areas. Dr. Iago Galdston of the New York Academy of Medicine, editor of the volume, introduces the topic theme with the statement that the traditional order (in medicine) has failed. Dr. Galdston concludes that the medical historian has the obligation to illuminate



the origin of this predicament so that we may be better able to anticipate the future and that in this illumination lies the attestation of the utility of medical history.

In the paper "Purposes and Values of Medical History" Dr George Rosen of the Columbia University School of Public Health notes that even though modern man lives in a scientific age he is nevertheless incorrigibly historical in his outlook. Dr Owse Temkin of the Johns Hopkins University in "A Critique of Medical Historiography" takes historiography to task with these words: "I do not care whether you write as historians or doctors but let me tell you that what you write is good for I want to profit by my reading." Dr Gregory Zilboorg also of the New York Academy of Medicine concludes that there is no such thing as objective history or objective historiography; that events are always interpreted in terms of the times and that in the serious world crisis of today it is more important than ever to teach the history of medicine as to place current events in historical perspective. Dr Edw. H. Ackerknecht of the University of Wisconsin Medical School concludes that unless the teaching of medical history is put on a firm basis the serious spoils for medical education will have strengthened the tendency toward the transformation of the doctor into a diagnostic and therapeutic technician. The final paper "Historians, Empiricists and Practitioners" by Dr Paul Schrecker discusses what the historian and what he is not.

Provocative and stimulating this little volume should be rewarding to the physician who is interested in medicine as an art as well as a science.—*MAE M. LINK, Ph.D.*

PRINCIPLES OF INTERNAL MEDICINE Ed T R H rr R ym d  
D Ad m l L B It J W H m H R k G g W Th m  
d M M W t b 3d d t 1839 p g ll tr d Th Bl k  
D M G w H ll Book C mp y In N w Y k N Y 1958  
P \$18.50

This large 1 800-page textbook of medicine may be obtained as a single volume or in two smaller separate volumes. There are six editors, each a well known clinician, investigating and teaching. There are 92 additional contributors, most of whom are faculty members of various medical schools.

The format and organization of this third edition is similar to the second edition. A few new chapters have been added and many sections have been edited or rewritten. The materials presented in a clear, direct and detailed manner and there are many outstanding sections in this book. Each of the editors has made extensive contributions in his own specialized field and the combined effort of all have produced an up-to-date, authoritative, fundamental textbook on the principles of internal medicine.

This book is unique standard textbook of medicine Basically the author attempts to present material in the same order provided student by a school curriculum The early chapters deal with the cad

nal manifestations of disease such as pain fever jaundice weight alterations et cetera and then take up the biologic considerations metabolic and endocrine disorders chemical physical and biological agents and diseases associated with reactions to stress and to antigenic substances This part of the book with stress on the correlation of the basic sciences to medicine is excellent It deals with pathologic physiology and metabolic disturbances as well as with disorders of nervous function with both the psychiatric and neurologic concepts integrated

The latter half of the book considers diseases of the organ systems In order not to repeat there are many references to related items which are discussed in other sections of the book Some may object to such a cross reference system however it should prove a more adequate coverage of a disease state which has numerous ramifications than an attempt at a complete treatise on each disease entity

An appendix gives laboratory values of clinical importance

The only minor criticism offered is that some discussions of treatment of a disease are of a general nature omitting details or failing to discriminate between the better and the less effective remedies

This book is most enthusiastically recommended as a text or reference work for those students and physicians interested in the specialty of internal medicine —DOSS O LYNN Col MC USA

ADVANCES IN ELECTROCARDIOGRAPHY edited by Charles E. Kossmann  
B S M D M d Sc D F A C P 280 pages illustrated Gune &  
Stratton Inc New York N Y 1958 Price \$6 75

This monograph evolved from the lectures given as the course of "advanced electrocardiography" in the postgraduate division of New York University at intervals since 1947 The book is divided into five parts The first is an excellent discussion of the physiology of the source of potential and the bio-electrics of myocardial cells The dynamics of the sodium pump theory as the origin of the trans membrane potential and its explanation of the action of autonomic nerves and chemical moderators is very well summarized Part two discusses the electrical field of the heart on the basis of the dipole theory source of potential The character of this electrical field in the irregular shaped volume conductor and the character of the conducting medium is developed with some rather involved mathematics This leads to a discussion of the present status of plain and semi orthogonal system of vectorcardiography The third part is an integrated discussion of the present concepts of the spread of excitation and recovery This part begins with a discussion of the endocardial myocardial and epicardial leads and proceeds into a well illustrated and timely essay on intraventricular conduction including bundle branch block parietal block incomplete block and ventricular hypertrophy This discussion is followed by a chapter on myocardial injury and the electrocardiographic interpretation of congenital heart disease The fourth part discusses the current concepts of the mechanisms of normal rhythm

and dy rhythm as Th fifth p rt an exc llent h t mm ry The auth editor and h s contributors have concisely present d the m jo fundamental th oies nd cur t tr ds The mathem tic l develop m nt in places assumes the reader is famili r with both trigonometry nd c lculus and is somewh t slow re ding for those not cu rent i the e ubj ct The review of this bo k gives o th fe ling that he h s ouch d b o e again on th ubj ct of l ctrocardi ogr phy The mo ograph will appeal to cardiolog t ad hould timu l te w d int rest among all internists

—WILLIAM D PRESTON C L USAF (MC)

PSYCHOENDOCRINOLOGY d t d by M R s M D D S 208 p g  
ll t d Gru & S tt l N w Y k N Y 1958 P \$7 00

Th utho s p nt a theory of endocri e psychi try which inte el t s person lity patt n emerg ncy tu tion and endocrine qul brium—nd l the dependence of person lity p tt n nd endocrine fun t n on genetic fa to Th th t cl o t of rm expl ns many c ntradict o nd ed t wuld pp to e pl n all the d fficulties th t h ve beset p ych at t Th uth r m k a plea fo nd cr ne e lu t on and for appropriate treatment to restore endocrine b lance If me t lly d sturbed patient should prove not t be in h monal imb l ce the th pist h s his ch ice (1) ho p t l iz tion and t have of th m lves normaliz d the mbal ce (2) p sent t hn cs are ot d l c t enough t d m nstrate the im b lance (3) ery ind d l ha h s own p tt n f ho m eq lib r m nd emotion l ch g may be ass t d with ce di gly m ll variations

Th bo k h s numb r of glari g typogr phic erro Th number of p tients dealt with m ll Results h not been h cked gainst contr l gr p A m nt of r p n e to tr atm nt depends n cl n c l judgm nt d a und ably ubje tive

—SAMUEL V THOMPSON C pt MC USN

MODERN TRENDS IN GASTRO-ENTEROLOGY (Se d Se ) d t d by  
F A ry J M D F R C P F w d by C F W Ill gw th  
439 p g ll t t d Pul B Hoeb I M d l B k D p m  
f H rpe & B h N w Y k N Y 1958 P \$16<sub>1</sub>

This excellent public tion and it c mpanion volume published few years go should be in the libr ry of every g st enterologist Although th ed tor t te th t the work n o sen e nt ded to be a comprehen ve tre tie on gastroenterology the book along w th the e l er v lume by th s me editor ctually co ers th mo t im portant aspects of the alim ntary tr ct nd ts dise se The work is essentially a series of s pa t t tis gastroente ological sub j cts A atomi ts phy iol gists pharmacologist radiol gists phy sicians ad surgeons e all l t d s contribut ry author

Th bo k s l gely th p duction of British ad Australia uthor ries although few chapte were w tte by American and Swedish clinicians It ofte h s been cl med th t most t xtbooks of medic ne

are obsolete before they are published. This allegation hardly applies here. To a surprising degree the most recent advances in alimentary tract diseases are presented.

In the opinion of this reviewer the chapter on carcinoid tumors by Waldenstrom and his colleagues is the finest presentation of that subject available today. The sections on steatorrhea and the blind loop syndrome and massive resection of the small intestine were especially good. It is obvious that Bockus and his Philadelphia group do not share the enthusiasm for steroids in the treatment of ulcerative colitis that Kirsner and the Chicago group do. The British surgeon Brooke has had a wide experience with ulcerative colitis. One gathers that he favors earlier surgery for this disease than do such American authorities as Bargen and others. Cummack's chapter on radiology of the biliary tract is excellent. He seems to have had greater success with intravenous cholecystography than most radiologists on this side of the Atlantic. Jones and Tanner evaluate the standard surgical operations for peptic ulcer. They are more enthusiastic advocates of the Billroth II procedure than most American surgeons. Howat's section on the tests of pancreatic function was most comprehensive and informative but the diagnosis of chronic relapsing pancreatitis still presents many difficulties.

The illustrations, photographs, statistical tables, and colored plates of the book are excellent, and the reproductions of x-ray films are especially clear. Each chapter is followed by an extensive bibliography. This work is unequivocally recommended for all who deal with diseases of the alimentary tract. —EMMETT L. KEHOE Col MC USA

CLINICAL STUDIES IN CULTURE CONFLICT. Edited by George Sewall. Pp. D 598. pages illustrated. The Ronald Press Company. New York. N.Y. 1958. Price \$7.

Most students of human behavior acknowledge the importance of cultural forces in the study of personality, in emphasizing the need for understanding an individual in terms of his own cultural frame of reference. The paucity of empirical data in this new field of learning has prompted the presentation of case material to help make concrete some of the specific ways in which culture may affect personality. Those who have accepted cultural relativism in behavior pathology will welcome this casebook of studies as an obvious attempt at spelling out in detail some of the processes involved in handling diagnosis and treatment of problems which involve culture disturbances. A book for clinicians on the psychology of minority groups, it presents 20 clinical case studies by 24 contributors, most of whom are psychologists, psychiatrists, and anthropologists. A wide range of psychopathology is covered by the book to demonstrate the cultural complications in the diagnosis and treatment of a variety of conditions. Treatment procedures utilized were broadly psychoanalytical (neofreudian) but the particular therapeutic approach varied from brief supportive measures to deeper analysis depending on the needs of the particular case. The case reports represent a multidisciplinary

attack of the clinical team collaborating in this field of socioclinical research. The book should be of value to any member of the clinical team. It should alert him to recognize the importance of cultural forces in the patient's background. The volume is intended primarily as a diagnostic aid designed to fill the need for a case book of clinical studies in culture conflict.—FRANKILLIAN J. LECHE, USAF (MSC)

ORR'S OPERATIONS OF GENERAL SURGERY by G. A. H. G. M. D.  
F. A. C. S. and Th. M. G. O. J. M. D. F. A. C. S. 3d ed.  
1016 p. g. with 1990 illustrations. 835 figures. W. B.  
S. and C. Company Phila. Pa. 1958. Pr. \$20.

This lengthy book is a monument to master surgeon Thomas G. Orr, recently deceased Professor of Surgery of the University of Kansas School of Medicine. It is also a remembrance of the golden era of general surgery before cannibalization and maiming were brought about by specialization. With no less courage than the master general surgeons of the past, the text boldly presents most of the surgical operations commonly performed on the human body. First brought out in 1944 by the senior Orr, this revised third edition has been completed by two of his former students, one of whom is his son. The original pattern and substance has been faithfully retained—in fact the authors have literally included some of the original dogma which is not currently acceptable. Thus in 1944, for example, they still proclaimed the superiority of silk suture material and advocate the packing of wounds with vessel gauze despite waning enthusiasm elsewhere.

However, there is much material of lasting importance which is properly presented. Wound healing is the subject of the opening chapter and this choice testimony in its life of the sound quality of the senior Orr. The important subject is given the emphasis and treatment warranted.

There are sections on general considerations and also on dangers and safeguards in connection with the operations described. These excellent and valuable additions make the book more than a mere surgical atlas; it is really a textbook of surgery emphasizing technical considerations.

The extent of this undertaking attempting to describe such a multitude of surgical procedures is of such magnitude as to raise the question as to whether a single volume can adequately contain all the important surgical procedures performed at present and whether any two general surgeons can properly select the procedures to be included. In general, the authors have succeeded admirably but there are indications here and there that selection by specialists might have been more advantageous. For example, the choice of Ariens' article in preference to Urban's ignores the original author with the widest experience and best description available of en bloc intestinal mammary ecternal nodal excision combined with radical mastectomy. Moreover, the procedure described is not only inadequate but im-

possible since the chest wall defect cannot be closed by drawing the ribs together transversely as described

Most illustrations are clear and easy to follow. An exception is the series on total laryngectomy which has lost so much by reproduction as to be practically worthless in supporting the excellent descriptive text of this procedure

This book should be of interest and value to medical students in giving them some understanding of operative procedures. A junior resident in general surgery could find it helpful as would general practitioners called upon for emergency surgery. As a single volume with such extensive coverage of the entire surgical field it would certainly be most welcome in the pack of the isolated physician no matter what his skill or training. —ROALD N GRANT Capt MC USN

REGIONAL ILEITIS by *Burnell B Crohn* M D and *Harry Yarnis* M D with special contributions by *Richard H Maheshak* M D and *David A Turner* Ph D 2d revised edition 239 pages illustrated Grune and Stratton Inc New York N Y 1958 Price \$7 25

Twenty five years of experience with 676 personally observed cases of regional enteritis is recorded and analyzed in this monograph by the man who has given his name to the malady. It is now recognized that the disease is not uncommon that it may affect not only the terminal ileum but also any portion of the enteric canal from esophagus to colon. Combined ileocolitis was seen in 64 cases, diffuse ileojejunitis in 70 cases while the remaining 542 cases were classified as regional or terminal ileitis.

The history, etiologic factors and pathology are discussed. There is an excellent presentation of the clinical features of the disease, its complications and diagnosis. Medical management is detailed, the various indications for surgery explained and the experience with different surgical procedures is discussed. A number of tables are used to present the data on these cases. About 20 per cent escaped operation and half of these were "well" without recurrence at the time of writing. The surgical results were good in 60 to 70 per cent and 30 per cent had recurrence of the disease. The short circuiting operation is preferred to resection of the diseased bowel. Separate chapters are used to describe acute ileitis, ileojejunitis and ileocolitis. Medical therapy is urged for these forms of the disease in view of the poor results of surgical measures.

The authors have presented in a useful fashion their knowledge and the results of their experience in treating a most difficult and discouraging disease. Much has been added since the first edition appeared in 1949, namely longer follow up of some patients, a wider and more detailed description of the disease and several new measures useful in medical therapy. Physicians who treat patients with abdominal complaints will find this book useful, all will find it interesting.

—BENJAMIN H SULLIVAN J Col MC USA

ANNALS OF THE NEW YORK ACADEMY OF SCIENCES V l 68, A t 3  
 p g 657 1266 Apr l 24, 1958 Ed t Ch f Ott V St W b t l k  
 M g g Ed t F k l N F A t Ed t s M g t  
 P C m d F S St b l Comp r t Cl l d B l g l  
 Eff ts f Alkyl t g Ag C l r g Ed t D d A K m / ky  
 609 p g illust t d Th N w Y k A d my f S N w Y k  
 N Y 1958

The papers contained in this volume were presented at a conference on alkylating agents in 1957. As with most annual of the Academy it contains wealth of information. Detailed reactions, preparative methods, and the fundamental characteristic of alkylating agents are covered, including r diomimetic agents. Speakers also covered the pathologic and hematologic effects of numerous alkylating agents and their pharmacological activity, distribution and fate. Of special interest to the physician are the large number of titles dealing with clinical trials of the agents in lymphoma, leukemia, and bronchogenic carcinoma. Two excellent papers are those describing recommended procedure for clinical trials of alkylating agents and a summary report of the status of alkylating agents in clinical cancer chemotherapy. All of the papers are well documented and illustrated. The article would seem a must for anyone concerned working in the cancer chemotherapy field. —DAVID F. HERSEY, C pt, USAF (MSC)

THE YEAR BOOK OF ENDOCRINOLOGY (1957-1958 Y Book S )  
 d t d by G l b t S G d M D Ph D F A C P 381 p g  
 ll t d Th Y Book P b l h r I c Ch g Ill 1958  
 P \$7.50

The articles abstracted in this volume have been well selected and are presented in a concise and clear manner. The abstracts represent the more important recent articles from the American and foreign literature pertaining to clinical and investigative endocrinology. An effort has been made by the editor to review articles not generally available to most American physicians. This volume is not intended to serve as a textbook of endocrinology but rather as a synopsis of the recently published literature on the subject. As a result, some aspects of endocrinology are not thoroughly discussed, however, the text covers the vast majority of the facets in the field of endocrinology.

This excellent summary of the recent literature pertaining to endocrinology should be included in the libraries of endocrinologists, internists, obstetric and gynecologists, as well as all teaching hospital. —RALPH D. ROSS, C pt, USN

THE YEAR BOOK OF ORTHOPEDICS AND TRAUMATIC SURGERY (1957-1958 Y ar Book Ser ) edited by Edward L. Campbell, M D, F A C S, F I C, S, W h PLASTIC SURGERY d t d by V l Owen, M D, F A C S, F I C, S 463 p g ll t t d Th Y B k P b l h I Ch g Ill 1958 P \$7.50

This yearbook is an interesting stimulating volume containing the usual orthopedic reviews of interesting and timely literature for the past year, as well as a new section on orthoplastic surgery. The subjects reviewed in the plastic surgery section which is edited by Dr

Neal Owens Professor of Plastic Surgery at Tulane University School of Medicine includes such subjects as reconstruction tissue transplants burns congenital anomalies neoplasms cosmetic and miscellany This is a most welcome addition to the yearbook as many of the overlapping problems of the orthopedic and plastic surgeons are reviewed in a terse pertinent manner

There are 59 footnotes by the editors following various articles and these are concise brief and stimulating as they constantly refer us to a review of fundamental principles of surgery

The usual yearbook quiz is included and its 21 questions make an introduction to this volume somewhat exciting and interesting For the busy surgeon this book represents a condensation of excellent literature review which he would never quite find time enough to sift for himself The yearly chapter entitled "Geriatric Orthopedics" has again been included in the survey It is especially recommended for residents in training —*HAROLD S McBURVEY Col MC USA*

THE YEAR BOOK OF NEUROLOGY PSYCHIATRY AND NEUROSURGERY (1957-1958 Year Book Series) edited by *Roland P Mackay M D* *S Bernard Wortis M D* and *Oscar Sugar M D* 624 page illustrated The Year Book Publisher Inc Chicago Ill 1958 Price \$8

This is essentially a reference work It presents excellent summaries of recent articles from American and foreign periodicals that seemed important to the editors they must be congratulated on their wisdom in sorting the wheat from the chaff Especially welcome are the pithy editorial comments that are added as footnotes to some of the abstracts Equally welcome is the editors mention of recent worthwhile books in the several fields covered as well as Dr Wortis suggestion as to several articles which should be read in full rather than in abstracted form

This volume keeps us informed on such diverse subjects as current theories of multiple sclerosis Heath's work on the isolation of tauraxin from schizophrenics Aberfeldt's serum test for schizophrenia and current opinions on sympathectomy Almost all physicians will find useful the chart and table listing all the current tranquilizing drugs and other psychopharmacological agents and their areas of usefulness This yearbook fulfills a definite need mostly for the busy specialist and resident

—*JOHN F McMULLIN Capt MC, USN*

THE YEAR BOOK OF DERMATOLOGY AND SYPHILOLOGY (1957-1958 Year Book Series) edited by *Rudolf L Baer M D* and *Victor H Wulf M D* 492 page illustrated The Year Book Publisher Inc Chicago Ill 1958 Price \$8

This is the usual fine compilation of abstracts and reviews of leading dermatologic articles that appeared in the literature between 1956 and late 1957 The book contains a total of 377 articles reviewed in abstract together with editorial comments The lead article continues



as Part 2 The Editors Review of Allergic Eczematous Contact Dermatitis of which Part 1 appeared in the 1956 1957 Year Book

Of the 377 articles abstracted only about 100 had no editorial comment In these it was obvious from reading the abstract that no comment was necessary These comments are quite worthwhile as the editors note any changes in the subject matter or treatment wherever necessary thus giving the editors a chance to assert their opinion and to point out certain simple truths which should be obvious but may have been long forgotten or overlooked In addition to this they provide stimulating food for thought for further studies in research

Another important change in this Year Book is that the editors have placed some of the abstracts or investigative studies with the clinical reports to which they pertain rather than all being included in one chapter as was done previously As the editors state this should improve the usefulness of the book The only major shortcoming appears to be that there is such a time lag between the appearance of the original article and its review and abstraction in this volume This of course is understandable although regrettable The editor acknowledges this fact and in the discussion on the use of the new corticosteroids methylprednisolone and triamcinolone points out that although these drugs have been given extensive clinical trial publications regarding their dermatologic effects have not as yet appeared in time to permit inclusion in this volume This is a worthwhile quick reference handbook which should be in every dermatologist's library and because of the material tables and discussion in the lead article should appeal equally to internists allergists and industrial physicians or only for reference but for general reading from time to time

—EARL S HALLINGR JR J L C I MC USA

SKIN GRAFTING by J m Berrill Brown M D and Frank M D with M D  
3d ed 411 p g 328 figs d 6 1 pl t J B Lippincott  
C m p y Phila d lph Pa 1958 P \$15

This book is written for the resident the general surgeon and the general practitioner It is a delightful authoritative presentation of the general subject of skin grafting by authors with wide experience Burns trauma and deformities are covered adequately Various types of grafts are discussed with consideration of why they work where each type is most valuable and what the pitfalls are The reader is told how and where to cut grafts of various types for various purposes how they should be applied how to prepare the recipient area and how to care for both the donor and recipient sites postoperatively Repair of various regions of the body and defects resulting from various causes and the faults of certain types of grafts are explained Moreover is the mistake made of considering the human organism as a mere platform on which to graft sheets of skin Equipment and methods are considered in enough detail to permit a physician to establish his own skin bank and adequately graft his needy patients using autografts or homografts Explanation of both practical and fundamental

... clear occasionally humorous, and never is the... complicated detailed and unnecessarily myste... in which some plastic surgeons shroud their specialty. This book is a contribution to the library of any physician who is or a specialist in plastic surgery but who may, on occasion be required to do repairs in the repair of defects.

—DONS WENGER Col USAF (MC)

**PEDIATRIC GYNECOLOGY** With Sections on Urology and Proctology by *Grafie C. Schauffler M.D.* 4th edition 349 pages illustrated The Year Book Publishers Inc Chicago Ill 1958 Price \$9

The author states in the foreword that the present volume is an... complete rewriting of the previous edition. In reviewing this book I had to take exception to this remark because except for the addition of a new and short chapter on "The Intersexes and Pseudomonism" the volume is almost word for word a copy of the third edition. The similarity was so marked that one can turn from a subject in the fourth edition to the same subject in the third edition and read on without any interruption in the train of thought. This is likewise true for the list of illustrations.

It is believed that Dr Schauffler has not sufficiently emphasized the necessity and need for cultures in the child or infant before a diagnosis of gonorrheal infection is made—relying too much on smear diagnosis.

In my opinion the owner of the third edition would hardly be justified in purchasing the fourth edition because of the very slight difference in content. Otherwise *Pediatric Gynecology* would be most useful as a reference for the resident in pediatrics.

—HENRY J HUNTER Capt MC USAF

**MODERN CLINICAL PSYCHIATRY** by *Arthur P Noyes M.D.* and *William C Kolb M.D.* 5th edition 694 pages W B Saunders Company Philadelphia Pa 1958 Price \$8

In this day of rapid advances in the therapy of mental disease standard texts on psychiatry are soon outdated. Such was the situation with Noyes' excellent fourth edition which appeared in 1954. In the fifth edition the authors have incorporated all the latest developments in treatment including drug therapy. The format of the book has been changed slightly and almost all chapters have been completely rewritten. The book now has a completely new format. The authors are Professor of Psychiatry, Columbia University, New York, and the note that the word "psychiatry" is used in the title, and the this method of therapy is used in the text. In the text the change of phenomena are noted with interest, and the fact that all of these concerns of the author are noted. The book is a very thorough and shattered... the text... highly recommended.

PHYSICS FOR THE ANAESTHETIST 1 l d g S e t EXPLOSIONS  
 by S R b t M l t b D M F R C. S. E F F A R C. S M D  
 (hon ) B A d A l x - M l l W l l m W M b M A  
 M B B S. F F A R C S. d H G E p t M A Ph D  
 F F A R C. S. 2d d t 443 p g l l t t d by M M M L ty  
 d M M B k Ch l C Th m P b l h Sp g f l d l l l  
 1958 P \$15 50

Since the first edition in 1947 this volume has been completely re-vised and a large section on explosions has been added. Satisfactorily referenced, the excellent illustrations include diagrams and photographs of early and modern anaesthesia equipment. The author reviews the physical attributes of liquids and gases and their effect on clinical response during anaesthesia. The functions of many items of equipment under clinical conditions are explained by diagram and illustration of the component of various types: reducing valves, flowmeters, mixing chambers, dividers, inter al and external respiration, discussed from the standpoint of osmosis, solubility and the diffusion of gases. The last third of the book is devoted to a comprehensive presentation of the factors which contribute to fires and explosions. Several approaches are offered to the prevention of the anaesthetic disasters. The publication offers a practical contribution to the anaesthesiologist, the anesthetist, the anesthesiologist, the physicist and the physical characteristics of the commonly used gases, liquids and vapors. It offers a valuable source of ready reference for the student as well as the expert and would make a useful addition to the library of any physician who has occasion to enter a surgical suite. —ROBERT F. CORWIN C I USAF (MC)

VETERINARY ANAESTHESIA by J h G W g h t 4 h d n 317 p g  
 l l r a d Th W l l m & W l k C m p y B l m M d 1957  
 P \$6 75

This book has a reputation as one of the standard texts on veterinary anaesthesia. The fourth edition, while retaining most of the material from previous editions, has been expanded to discuss and evaluate several methods and agents which have been developed since the publication of the third edition in 1952. This includes some of the ether, etheralizers and the curare-like drugs. A refreshing aspect of the book is the author's comments and discussions of many of the agents and methods discussed. They include many valuable practical considerations. He has surveyed the available publications on the subject and incorporated the experience and observations of others in this field. This book is a valuable reference for both the student and the practitioner. It provides a concise source of information for the practitioner who does not routinely work on all species of animals in that it gives him comprehensive discussions of the methods and agents which he is most likely to be most adept at using for most of those species with which he commonly comes in contact. The American reader will suffer some confusion because of the variations in proprietary drug names. Also, some of the drugs and equipment which are discussed are not readily available in the American market.

—ROBERT M. NIMS Lt C I VC USA

**OPHTHALMIC PLASTIC SURGERY** by *Sidney A. Fox* M S (Ophth) M D  
F A C S 2d revised edition 324 pages illustrated Grune & Stratton  
Inc New York N Y 1958 Price \$15

Designed for the practicing ophthalmologist this book describes in an understandable manner the basic classical operations commonly used in everyday practice. The brief review of anatomy in the beginning is excellent for the occasional operator. Discussions of various surgical techniques are brief but clear and to the point. The author not only describes classical procedures but he inserts minor changes here and there which in his experience have ensured better results. His double triangle procedure for correction of entropion is simple and seems easy to perform. When he describes several procedures for correction of a certain defect he criticizes the results of each procedure and gives specific indications for each operation. Illustrations are numerous and realistic. This book does not include all the possible operations for the ophthalmic plastic surgeon but it describes most of them that give satisfactory results. It is recommended for all practicing ophthalmologists and medical libraries. —JAMES L. FUELLING Capt MC USN

**SURGERY OF THE CHEST** A Handbook of Operative Surgery by *Julian Johnson* M D D Sc (Med) and *Charles A. K.* by M D 2d edition  
398 pages illustrated by *Edna Hill* The Year Book Publishers Inc  
Chicago Ill 1958 Price \$9.75

Drs Johnson and Kirby have enlarged their most excellent handbook and present what is believed to be an unexcelled concise well illustrated text. The enlargements consist almost entirely of new operations in cardiac surgery. In keeping with the first edition this book fills a true need and all who are interested in the subject of chest surgery will find it a valuable addition. To the residents in particular this book should find great usage.

—JAMES H. FORSEE Brig Gen. MC USA

**DENTAL CLINICS OF NORTH AMERICA** Symposium on The Interrelationship  
of Oral and Systemic Disease Edited by *L. E. B. K. D. D. S. M. D.* Con-  
sulting Editor 543 pages illustrated W B Saunders Company Phil-  
adelphia Pa 1958

The 25 contributors to the volume are outstanding authorities and their articles contain valuable and practical information. Because the interrelationships between oral and systemic disease are numerous and significant space does not permit a coverage of the many diseases, diagnostic procedures, treatments and other subjects considered. A valuable feature of the book is the inclusion at the end of most chapters of a list of pertinent bibliographic references. These references have been carefully selected so that the reader who wishes to develop a bibliography on any particular phase of the literature may do so. This book is recommended to the practicing dentist whose desire for knowledge and understanding transcends the ordinary dental knowledge. Also this book would be a valuable addition to the professional library of any practicing physician.

—THOMAS SALI F O J Capt USAF (DC)

DRUGS Thir N tur Ac d U by H rry B km M D 728 p g  
ill t t d W B S und Company Ph l d lph P 1958 P \$15

This is a unique textbook of pharmacology written for the undergraduate medical student. It is appreciably smaller than most of the books in common use with less than half the pages of some standard works. The style of presentation is different in several ways. For one it is written in the first person and for another the material is arranged in an unusual way. There is an interesting and entertaining initial chapter entitled "A justification of pharmacology and pharmacologists" followed by a section including the sources of drugs, the relation of structure to activity, the nature of drug action on the fate of drugs, factors affecting administration, drug addiction, drug sensitivity, and the preparation and writing of prescriptions. The subsequent organization is more conventional and is based primarily on organ systems and tissue. Figures and diagrams are abundant and the references at the end of each chapter are numerous and well chosen. The opinions of the author are frequently expressed but he is careful to separate opinion and conjecture from established facts. Attention is frequently called to extensive gaps in our knowledge of drug action and the urgent need for effective agents in certain cases. The book is intended to be very interesting and informative to medical and pre-medical students and delightful reading to the physician and medical professional interested in pharmacology. —PAUL K. SMITH C I USAFR

DIAGNOSTIC LABORATORY HEMATOLOGY by G. E. C. I.  
2d ed. d d larg d 250 p g ill t t d  
S t I N w Y rk N Y 1958 P \$6.50

This up-to-date revision of laboratory procedures is of unusual clinical physics and surgeons as well as for the clinical laboratory technician. The author presents his material in a practical detail with the clinical hematologic approach in mind. It is a concise and chief Dr. M. M. Wintrobe. The book is well organized. Contents. Among the topics is a description of the terminology of hemoglobin and the other red blood cells and those for platelets and white blood cells. The causes and forms of anemia and pancytopenia are listed for reference. The hemorrhagic disorder and the factors associated with it are discussed. The hemolytic diseases are thoroughly presented from a laboratory diagnostic aspect. The author states that in brain for the various studies it is important to use the proper anticoagulant. He recommends double oxalate or if platelets are to be determined, ethylenediamine tetraacetate (Versene). An especially useful section details the use of special blood smears and the use of bone marrow studies, various clinical conditions. The book with a report on the biochemistry of jaundice and blood and pigments and some of the special protein determinations and differential diagnosis of certain diseases. One interesting point brought forth is the limited value of the determination of erythrocyte sedimentation rate. —U. R. MERIKANGAS C I MC, USA



THE YEAR BOOK OF CANCER (1957 1958 Year Book Series) compiled and edited by R. d. Iph. L. Gl. k. J. B. S. M. D. M. Sc. (S. g. y.) D. Sc. (H. ), d. R. H. W. C. m. l. y. B. A. M. A. Ph. D. 523 p. g. 11 t. t. d. Th. Y. B. k. P. bl. h. I. Ch. g. Ill. 1958 P. c. \$8

THE PRACTICE OF NUCLEAR MEDICINE by W. I. am. H. Bl. hd. M. D. F. K. Bau. r. M. D. and Ben. d. t. C. Ph. D. I. t. od. t. by P. I. A. b. sold. Ph. D. F. r. w. d. by J. eph. F. R. M. D. 407 p. g. 11 t. r. t. d. Ch. l. C. Th. m. P. bl. he. Sp. gf. ld. Ill. 1958 P. r. c. \$12.50

CONGENITAL ANOMALIES OF THE HAND AND THEIR SURGICAL TREATMENT by A. th. J. ph. B. ky. M. D. D. D. S. Am. L. tur. S. P. bl. c. t. N. mb. 311 A. M. g. ph. Th. B. t. D. f. Am. n. L. t. Orth. p. d. Surg. ry. ed. t. d. by Ch. l. W. G. H. M. D. 165 p. g. 11 t. r. ed. Ch. l. C. Th. m. Sp. g. f. eld. Ill. 1958 P. \$5.75

LIVE AND LET LIVE Th. M. l. f. th. W. lf. d. R. p. t. by D. E. t. Ch. w. th. f. w. d. by S. J. b. W. lf. d. n. 125 p. g. Ph. lo. ph. c. l. L. b. ry. I. N. w. Y. k. N. Y. 1958 P. \$4.75

THE WAKING BRAIN by H. W. M. g. Ph. D. 137 p. g. 11 t. t. d. Ch. l. C. Th. m. P. bl. h. Sp. gf. ld. Ill. 1958 P. \$4.75

CLINICAL NEUROANATOMY NEUROPHYSIOLOGY AND NEUROLOGY with M. th. d. f. B. in. R. t. t. by L. H. m. M. D. 522 p. g. Ch. l. C. Th. m. P. bl. h. Sp. gf. ld. Ill. 1958 P. \$9.75

HOMOSEXUALITY TRANSVESTISM AND CHANGE OF SEX by E. g. d. S. t. b. M. D. 118 p. g. 11 t. r. t. d. Ch. l. C. Th. m. P. bl. h. Sp. gf. ld. Ill. 1958 P. c. \$3.50

PRINCIPLES OF RADIOGRAPHIC EXPOSURE AND PROCESSING by A. th. W. F. b. 2d. d. t. 284 p. g. 11 t. r. t. d. Ch. l. C. Th. m. P. bl. h. Sp. gf. ld. Ill. 1958 P. \$10.50

SIMPLE METHODS OF CONTRACEPTION A. A. m. t. f. th. Med. c. l. M. l. d. S. l. Impl. t. d. t. d. by W. f. ld. B. t. d. F. d. k. S. J. ff. w. th. f. w. d. by R. G. d. D. gl. M. D. 64 p. g. Pl. d. P. th. od. F. d. t. f. Am. N. w. Y. k. N. Y. 1958 S. gl. p. d. h. dl. g. l. bl. f. pt. f. 25 ch. tg. for. p. t. g.

HUMAN DISSECTION It. D. m. d. St. ggl. by A. M. L. k. M. D. Ph. D. 310 p. g. 11 t. t. d. Ch. l. C. Th. m. P. bl. h. Sp. gf. ld. Ill. 1958 P. \$6.50

BIBLIOGRAPHY OF INTERNATIONAL CONGRESSES OF MEDICAL SCIENCES prepared by W. J. B. b. p. und. th. p. f. h. C. l. f. I. t. mat. l. O. g. t. f. M. d. l. Scien. w. th. th. f. an. l. t. f. U. co. 238 p. g. Charl. C. Th. m. P. bl. sh. Spr. g. f. ld. Ill. 1958 P. \$5.50

DISCUSSIONS ON CHILD DEVELOPMENT A. C. d. t. of. th. B. l. g. l. P. y. h. l. g. l. and C. l. tur. l. App. h. t. th. U. d. tand. g. f. H. m. D. l. pm. t. d. B. h. ur. V. lum. 3 Th. P. d. g. f. th. Th. d. M. t. g. f. th. W. ld. H. l. th. O. gan. t. St. dy. G. p. o. th. P. y. h. b. o. l. g. l. D. l. pm. t. f. th. Ch. ld. G. 1955 Ed. t. J. M. T. M. D. D. S. P. M. d. B. b. l. l. b. l. der. 223 p. g. I. er. t. l. U. t. P. l. N. w. Y. k. N. Y. 1958 P. \$5

A DOCTOR SPEAKS HIS MIND by R. b. rt. l. L. M. D. 120 p. g. L. t. l. B. w. n. d. C. m. p. any. B. t. M. 1958 P. \$3

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The *United States Armed Forces Medical Journal* is devoted to the publication of original investigation, observation, and clinical experiences of interest to personnel of the medical service of the three military departments. Contributors who are affiliated with the Army or Air Force in a commissioned, enlisted, or civilian capacity should forward manuscripts in triplicate to their respective Surgeon General in accordance with existing regulations. Naval contributors may submit manuscript in triplicate either to their Surgeon General or directly to the Editor. When an article by a person in the naval service is accepted for publication, one of the triplicate copies will be forwarded by the Agency to the Secretary of the Navy, which will constitute compliance with regulation. Authors not affiliated with one of the armed services should send manuscript directly to the Editor. Whatever the channel of submission, the covering letter should state that the author desires the manuscript be given consideration for publication in the *Journal*. Accepted manuscripts become the property of the Armed Forces Medical Publication Agency.

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Fleming A, Young M Y, Suchet J and Rowe A J E. Penicillin content of blood serum after various doses of penicillin by various routes. *Lancet* 2: 616-94 No. 11 1944.

Cibot R C. Ierniciou and secondary anemia, chlorosis, and leukemia. In Oler W (editor). *Modern Medicine*. 3d edition. Lea & Febiger Philadelphia, Pa. 1937. Vol. 5 pp. 33-100.

### FIGURES AND TABLES

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n this issue



*Atherosclerosis*

*Viral Encephalomyelitis*

*Howard Bailey Tourniquet*

*Pasteurized Pooled Human Plasma*

*Splenoportography in Portal Hypertension*

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# UNITED STATES ARMED FORCES MEDICAL JOURNAL

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GOVERNMENT PRINTING OFFICE  
WASHINGTON 1958

## Monthly Message

At the invitation of the Turkish Government an International Nutrition Conference was held at Ankara on 14 15 and 16 April 1958. The nations represented were Turkey Iran Pakistan Iraq and the United States. The United Kingdom had expected to send representatives but they were unavoidably detained. Libya had been invited to participate but was unable to send delegates.

This is the second international conference of this sort the first having been held in Tehran last year at the invitation of the Iranian Government. Dr Arnold Schaefer the Executive Director of the Interdepartmental Committee on Nutrition for National Defense, is the Secretary of these conferences and arrangements each year are carried through by him and the host country. Both deserve much credit for the consummation of these extremely successful conferences. This year there were excellent papers by all countries represented with free discussion in fact so free that each day was not long enough.

The chairmanship rotated for each session as did the temporary secretary so that all countries had the opportunity to conduct the meetings. In all probability next year's session will be held in Pakistan where we can look forward to an equally good program because of the interest manifested in that country. Although the principal purpose of these meetings is the improvement of nutrition in the armed forces nevertheless interest soon spreads to the civilian groups. There is close cooperation throughout with our own International Cooperation Administration programs to assist materially in establishing food processing factories and providing instruction and advice for their management.

*Frank B Berry*

FRANK B BERRY M D  
Asst Secretary of Defense  
(Health and Medical)

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## Foreword

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FRANK B BERRY M D

A t t S t y f D f en (H alth and M d l)

MAJOR GENERAL SILAS B HAYS

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REAR ADMIRAL BARTHOLOMEW W HOGAN

S g G l U t d St t N y

MAJOR GENERAL DAN C OGLE

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# UNITED STATES ARMED FORCES MEDICAL JOURNAL

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## REVISED DEPENDENTS' MEDICARE PROGRAM

FRANK B. BERRY, M.D.

**I**N order that all members of the uniformed services, especially physicians, will be adequately informed about the major changes in the Medicare Program as a result of Congressional action effective 1 October 1958, it is important that the basic facts pertaining to these changes be made known through the *Journal*.

It is essential that the restrictions as to freedom of choice imposed on spouses and children of active duty service personnel and the reductions in authorized medical care be thoroughly familiar to those who are concerned in providing the medical care for dependents in service medical facilities. Unless this knowledge is available and known by our medical personnel, it may well complicate the administrative problems attendant to dependents seeking such care from civilian facilities.

It must be remembered

Written permission to obtain civilian medical care must be obtained only by those dependents residing with their sponsors or in an area in which the sponsor is assigned.

The reduction in authorized care involves all dependents, not only those residing with their sponsors but also those residing apart from their sponsors.

All medical officers should study carefully the changes in authorized care. Both of the above restrictions will divert dependents seeking medical care to service medical facilities. Every consideration to good physician-patient relationship should

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be encouraged. Everyone in the treatment facility dealing with these dependents—from the receptionist to the laboratory technician and especially all attendants—should be friendly, courteous, considerate and helpful to such patients.

The information included herein should be read and understood by everyone concerned with medical care of dependents of service personnel on active duty. To do so will help retain high morale as well as to provide optimum utilization of our uniformed services medical facilities.

The changes in the Medicare Program effective 1 October 1958 fall into two broad categories: (1) Restrictions on the use of civilian medical facilities for dependents residing with the service member on whom they are dependent and (2) Reductions of the authorized care and services provided from civilian sources for which the Government will pay.

To see precisely what dependents of members of the uniformed services may expect under the revised program, let us examine the program in detail.

#### ELIGIBILITY FOR CIVILIAN MEDICAL CARE

Some dependents are eligible for both civilian medical care and care in service facilities. For a dependent to be eligible, the sponsor must be on active duty or on active duty for training for a period of more than 30 consecutive days. The dependent must also bear one of the following relationships to the sponsor:

##### Lawful wife

Lawful husband if dependent on service wife for over one half of his support.

Unmarried legitimate child, adopted child or stepchild in one of the following categories: (1) Under 21 year of age; (2) over 21 but incapable of self support because of mental or physical incapacity that existed before the age of 21 and dependent on service member for over one half of support; or (3) under 23, enrolled in a full time course in an approved institution of higher learning and dependent on service member for over one half of support.

Eligibility of the dependent for civilian medical care ceases when the service member who is the sponsor dies, is discharged, divorced, retires, or is released from active duty. Eligibility also ends if the sponsor is dropped from the rolls of his service in desertion. If he dies while on active duty or while in a retired status, his dependents are still eligible for care at Armed Forces and U S Public Health Service medical facilities when space and staff are available.

For purpose of administering the revised Medicare Program, dependents who meet the above requirements are divided into two classes:

- 1 Dependents residing *apart* from sponsors
- 2 Dependents residing *with* sponsors

How does the revised Medicare Program affect each of these classes?

**Dependents Residing Apart from Sponsors** Dependents eligible for civilian medical care who reside apart from their sponsors may continue to choose between civilian facilities or a facility of the Armed Forces, or they may use a U S Public Health Service medical facility

Civilian physicians and hospitals, when providing care for dependents, will each furnish the dependent with a claim form (DA Form 1863 entitled "Statement of Services Provided by Civilian Medical Sources") to be filled in. When the dependent patient resides apart from the sponsor, item 4 on the claim form must indicate that the patient is residing apart from sponsor. If the attending physician requires the services of other physicians, an anesthetist or a private duty nurse while the dependent patient is in a civilian hospital, a DA Form 1863 must be completed for each of them. These claim forms also must indicate that the patient resides apart from sponsor.

When applying for civilian medical care, the dependent should first ask the physician if he will participate in the Medicare Program.

**Dependents Residing With Sponsors** Wives and dependent husbands and children of service members, who reside with their sponsors, are required to ascertain from a uniformed services authority whether the required care can be provided in a nearby service medical facility.

When the authorized care is *not* available from service medical facilities, the dependent must get a Medicare Permit (fig. 1) from the appropriate service authority to seek authorized civilian care. This permit allows the dependent to receive care authorized under the revised Medicare Program from civilian sources at Government expense and is for immediate use.

In some cases, Government paid medical care from civilian sources may be provided without a Medicare Permit. These are as follows:

- 1 In an acute emergency requiring immediate hospitalization at the nearest hospital in order to preserve life and prevent undue suffering. The attending physician must state on the claim form (DA Form 1863) or on an attachment to the claim form that the case is actually an acute emergency.

- 2 When the dependent is away from the area of the sponsor's household on a trip, the person signing item 14 on the claim will be required to make an entry in item 3 or 4 certifying that the dependent is on



trip. This exception is not to be used to circumvent restrictions on the use of Medicare Program.

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*Figur 1. Nødder og Perm*

3. A maternal patient (residing with sponsor) under the care of a physician or before 1 October 1958 may continue under this care provided that patient is checked the 15th week of pregnancy on or before that date. The attending physician will indicate on DA Form 1863 (attach to it) that the patient meets the above requirements. The hospital will also make a similar statement on its DA Form 1863.

4 I the case of defendant who was admitted to a civilian hospital before 2400 hours 30 September 1958 when the hospital care required for this claim terminated beyond 30 September 1958. The date of

admission shown by the hospital on the claim form must indicate that the admission occurred before 1 October 1958

5 When a dependent is receiving authorized care from a physician and is admitted to a civilian hospital before 2400 hours 30 September 1958 the dependent will be authorized such care by that civilian physician On the claim form the physician must show that the date of admission to the civilian hospital was before 1 October 1958

### CIVILIAN CARE PROVIDED

Effective 1 October 1958, the Government pays the major cost of the following services for those eligible dependents who meet the requirements for civilian medical care

Hospitalization in semiprivate accommodations (2 3 or 4 beds) not to exceed 365 days for each admission and the physicians bills during hospitalization for treatment of (1) acute medical conditions (2) contagious diseases (3) surgical emergencies (4) acute surgical conditions and (5) severe injuries during the acute phase

Laboratory and x ray tests and procedures during hospitalization

Complete obstetrical and maternity care including in hospital care of the newborn infant Infants delivered by civilian physicians in a home or an office may receive required authorized care on an outpatient basis during a period not to exceed 10 days following the date of delivery

### CIVILIAN MEDICAL CARE NOT PROVIDED

Effective 1 October 1958 the following care and services are not authorized from civilian sources

1 Treatment of fractures dislocations lacerations and other wounds not requiring hospitalization

2 One visit to a civilian physician whose services terminate before or upon hospitalization of the patient

3 Pre- and post surgical tests and procedures such as roentgenograms and laboratory tests performed on an outpatient basis except in maternity cases

4 Two visits by a physician to examine an infant within 60 days after birth The hospital care of a newborn infant is still provided as part of complete maternity care

5 Treatment of acute emotional disorders Care of an acute emotional disorder may be furnished to a spouse or child however if required but only during the period of hospitalization of that spouse or child for a condition that *does* qualify as authorized care

C Medical and surgical care that can be planned Medical or surgical care that is desired or requested by the patient which in the opinion of the responsible medical authority can be planned later scheduled and effectively treated at a later date without detriment to the patient

Examples are diagnostic surveys cosmetic surgery reconstructive surgery tonsillectomies uncomplicated hernia operations for relieving or producing sterility and appendectomies when not an acute surgical problem

7 Chronic disease except for acute exacerbation or acute complications requiring treatment in a hospital

8 Dental care This means personal nursing care normally provided in an institution such as a nursing or convalescent home

9 Ambulance service (May be provided by service facilities under limited circumstance)

10 Medical supports or aids Dependents who need a prosthesis hearing aid orthopedic footwear spectacles will have to buy them at their own expense Outside continental United States in a prescribed remote area within the United States where such appliances are not available from private sources such items may be sold to dependents if available from Government stock at cost

### CIVILIAN OUTPATIENT CARE

Outpatient care from civilian sources is restricted to authorized obstetrical and maternity care For all other outpatient care at Government expense dependents must use uniformed services medical facilities

### DENTAL CARE

The provisions for dental care remain unchanged Generally the Government will not pay for civilian dental care Dental treatment is provided only to patients who are hospitalized for otherwise authorized care as a necessary part of the treatment of the basic medical or surgical condition requiring their hospitalization It does not include the cost of artificial teeth bridges fillings teeth straightening or prolonged treatment of the gums

At Armed Forces and U S Public Health Service medical facilities dental care is provided as follows

#### 1 Continental United States

1 In an emergency to relieve pain and undue suffering Permanent fillings bridges and dentures are not authorized

2 If required for treatment of a medical or surgical condition

3 Dental care in areas designated military facilities available basis

#### Outside continental United States

1 Dental care in a facility available basis

### CARE IN SERVICE MEDICAL FACILITIES

If medical staff space and facilities are available the medical services of the uniformed services will provide care for all eligible dependents as follows

Diagnosis  
Treatment of

- 1 Acute medical conditions
- 2 Surgical conditions
- 3 Contagious diseases
- 4 Acute emergencies of any nature

Immunization

Maternity and infant care

### MEDICAL CARE OVERSEAS

As a general rule, dependents will receive required care from service medical facilities when they are outside continental United States, Alaska, Hawaii, and Puerto Rico. If Armed Forces or U S Public Health Service facilities are lacking or inadequate, civilian medical care may be arranged for at the expense of the U S Government. Dependents residing in overseas areas where service medical care cannot be provided may obtain full information from the appropriate overseas commander or from the nearest service installation on how to obtain medical care from professionally acceptable local civilian sources.

### ELIGIBILITY FOR MILITARY CARE

Dependents are eligible for care in service medical facilities if they bear one of these relationships to a retired service member, to a service member who died while serving on active duty for a period of more than 30 days, or to a deceased retired service member:

Lawful wife

Lawful husband, if dependent

Unmarried widow

Unmarried widower, if dependent

Unmarried legitimate child, adopted child or stepchild if such child has not passed his 21st birthday. See page 1406 for exceptions covering those past 21 years of age.

Parent or parent in law, if dependent and if residing in a dwelling place provided or maintained by the service member or retired service member. (A parent or parent in law of an active duty service member is also qualified for care at service facilities if he meets the above requirements.)

### IDENTIFICATION

When applying for any kind of medical care to a service or civilian facility, or to a civilian physician, dependents are required to present a Uniformed Services Identification and Privilege Card (DD Form 1173) as proof of eligibility for medical care.

All eligible dependents except children under 10 years of age may obtain a card. In some cases such as a child living apart from his parents a card may be issued even for a child under 10. In the case of a child under 10 the parent or guardian must furnish proper identification and certify as to the child's eligibility.

Dependents residing with their sponsors will receive their cards through their sponsors. The sponsor will fill out the necessary application form and submit it to his commanding officer. Sponsors residing apart from their dependents may send the completed application form to their dependents.

If the sponsor is unable or declines to fill out the application form his dependent can obtain the necessary application form at any service installation fill in as much information as possible and submit it to the sponsor's commanding officer for completion and verification.

Dependents of service members who died while on active duty or while in a retired status may obtain an application for the card from a nearby service facility by applying there in person or requesting it by mail. Information on how to fill out the form and what certificates must accompany it can be obtained at the same time.

The completed application form must be taken to a uniformed service facility. If the necessary equipment to produce the card is not available there the dependent will be advised where to obtain the card. Dependents who cannot visit a service facility that can issue the card may request it by mail.

The card must be turned in (1) when it expires (2) when a new card is issued (3) when the sponsor dies is discharged retires or is released from active duty or (4) when the dependency status is otherwise ended. When a card is lost the loss should be reported immediately so it may be replaced and the services may be on the alert against its being used improperly by someone who finds it.

If a person uses a card to obtain medical care to which he is not entitled a fine of up to \$10 000 and imprisonment for up to 5 years may be imposed on the offender. A dependent who allows another person to use his card unlawfully may be subject to the same penalties. Damage to or indications of tampering with the laminated card makes it invalid.

#### A WORD OF CAUTION

Dependent residing with their sponsors in addition to furnishing proper identification must present a Medicare Permit to the source of civilian care except under those circumstances previously stated.

Except in an emergency, eligible dependents seeking medical care from civilian sources should make sure the physician and hospital are participating in the Medicare Program before beginning treatment

A physician participating in the program must be legally licensed and qualified to prescribe and administer all drugs, and to perform all surgical procedures

A hospital, to qualify under the Medicare Program, except in an emergency, must be engaged primarily in providing facilities for the surgical and medical diagnosis, treatment, and care of injured and sick persons by or under the supervision of two or more staff physicians or surgeons. It must also provide continuous 24 hour nursing service by registered graduate nurses

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### THE SHOTGUN CAPSULE

A few decades ago before medicine became as precise and scientific as it is today doctors prescriptions often consisted of six to eight or more ingredients many of which were more or less inert. The prescriptions were written in Latin and the mystery of the ingredients constituted part of their virtue. Gradually most of this sort of unscientific and meaningless procedure was abandoned. Professors of medicine and of pharmacology taught students to use simple drugs for precise reasons and for definite periods. Gradually with the intense development of chemotherapy of antibiotic therapy of antihistaminic therapy of endocrinologic therapy and of vitamin therapy there has been a mushrooming of drug manufacturers who are in desperate competition. The commercialistic factor has crept into therapeutics to such an extent that physicians everywhere are confused and misled by the literally thousands of drugs increasing in number daily. Dozens of expensive commercial brochures sample drugs and elegant preparations reach one's office daily and are promptly disposed of in the wastebasket. Many of these modern preparations are mixtures of drugs some of which are dangerous some of which are useless and most of which would be more intelligently given as separate drugs rather than in a shotgun capsule.

—CLAUDE E. FORKNER, M.D.

in *The New England Journal of Medicine*  
p. 439, Aug. 28, 1958

# ESSENTIAL HYPERLIPEMIA

GEORGE E GORSUCH L T MC USN

THE clinical condition manifested by an idiopathic familial hypertriglyceremia with varying levels of blood cholesterol and phospholipids is called essential hyperlipemia. The characteristic laboratory feature in this disease is milky white serum in the fasting state. In 1939 Bürger and Grütz described hyperlipemia, hepatosplenomegaly and xanthomatous eruption in a 12 year old boy believed by many to be the first reported case of essential or idiopathic hyperlipemia. The condition has been separated into a familial childhood type associated with hepatosplenomegaly and abdominal pain and a nonfamilial variety which frequently was without symptoms and sometimes associated with glycosuria.<sup>2</sup> This division is somewhat untenable at present and most authors now consider all forms simply as idiopathic or essential hyperlipemia. Over seventy cases have been noted thus far in the literature. The syndrome of a classical case of essential hyperlipemia includes (1) opaque white serum in the fasting state (2) a family history (3) recurrent abdominal pain (4) lipemia retinalis (5) hepatosplenomegaly (6) xanthoma of the skin and (7) an absence of other known causes of hypertriglyceremia.

The following case of essential hyperlipemia was observed for an 11 year period.

## CASE REPORT

A 40-year old Caucasian was admitted to this hospital on 24 April 1957 for evaluation of a blood pressure of 170/90 mm Hg and albuminuria which had been discovered during a routine physical examination.

Past history revealed that the patient had been in good health until sometime in 1946 at the age of 30 years. He was on active duty in the Navy when he sustained an episode of severe abdominal pain, back pain, chill, fever, nausea and vomiting. He eventually was hospitalized for 5 days at the U. S. Naval Hospital, Newport, R. I. where no definite diagnosis was established. He was readmitted to that hospital the later part of 1947 because of complaints of chest pain, fatigability and hot flashes. He had transient hypertension and albuminuria at that time. No diagnosis was established and the patient was again

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From U. S. N. Hospital, St. Clair County, Illinois and U. S. Naval Hospital, Bethesda, Md.

discharged to full duty He continued to have intermittent abdominal pain and stomach distress

In February 1948 the patient consulted his family physician A blood sample drawn at that time was "milky" and a biopsy performed on a lump found on the back of the patient's neck was reported as showing benign fat necrosis

In June 1948 this man was again admitted to the U S Naval Hospital Newport R I because of abdominal pain A laparotomy was performed and the peritoneal cavity was noted to be full of milky white fluid No other definite pathologic condition was described on the operative note The incision was closed quickly because of deterioration of the patient's condition on the operating table A blood sample taken during that admission was milky white and the previously noted history of milky serum was then disclosed to the attending physicians A sample of blood was sent to the laboratories of Dr S J Thannhauser and a report on this blood was as follows Total fatty acids 6 785 mg per 100 ml neutral fats 5 665 mg per 100 ml total phospholipids 771 mg per 100 ml total cholesterol 1 170 mg per 100 ml free cholesterol 256 mg per 100 ml cholesterol as esters 828 mg per 100 ml The patient's clinical course and laboratory findings were said to be typical of the picture of idiopathic hyperlipemia This patient was again discharged to duty on a low fat diet He continued to have recurrent episodes of abdominal pain In 1949 he was re-evaluated at the U S Naval Hospital Chelsea Mass where his serum was again noted to be milky

In April of 1952 he was admitted to U S Naval Hospital Portsmouth Va in an acutely ill condition He complained of severe generalized abdominal pain nausea vomiting and back pain A serum amylase on that admission was reported as normal Because of the patient's past history he was treated as having acute pancreatitis associated with essential hyperlipemia He responded very well When this patient's acute episode subsided and he was able to relax sufficiently a large mass was palpated in the right upper quadrant of his abdomen At exploratory laparotomy a large pseudocyst of the pancreas was found and drained The gallbladder contained many yellow cholesterol stones and it also was removed The patient apparently recovered fully and was returned to duty He remained well and had no symptoms referable either to hyperlipemia or pancreatitis Slight albuminuria had been noted in 1954 In 1955 he was hospitalized for labile hypertension at the U S Naval Hospital Newport R I for three days

There was no family history of diabetes The patient's father died of heart trouble at the age of 70 years and his mother died following a ruptured appendix at the age of 35 The two brothers and one sister were living and well with ages ranging from 33 to 44 years One brother had had a ruptured appendix One brother had hyperlipemia and hypercholesteremia All grandparents were over the age of 65 years at the time of their death and there was no family



history of xanthom tosis and no other history of xanthom tosis except as noted in the previous (February 1948) biopsy report

On the present admission system review revealed that the patient rarely ate fatty food but had no marked intolerance to it. His stools were normal in size, color, and consistency. There was no history of kidney disease except the previously noted albuminuria. There was no history of heavy alcohol intake.

Physical examination on admission revealed an obese sluggish appearing man with a florid complexion who did not appear acutely or chronically ill. His blood pressure was 130/80 mm Hg. His weight was 225 pounds. A fundoscopic examination was negative. There was no evidence of lipemia retinalis and there were no hypertensive or arterioclerotic changes. No xanthom was found on examination of the skin. The spleen was firm and slightly palpable three fingers breadth below the left costal margin. The liver also was firm and nontender four fingerbreadth below the right costal margin. The remainder of the physical examination was entirely negative.

Laboratory studies on admission revealed the following: Serum lipemia was 4 plus. The serum was creamy white. Total lipids 3550 mg per 100 ml, phospholipids 634 mg per 100 ml, total cholesterol 684 mg per 100 ml, cholesterol esters 410 mg per 100 ml. Thyroid function tests were within normal limits. Total protein was 12.1 grams (albumin 5.3 gm and globulin 6.8 gm) per 100 ml. An electrophoretic serum study revealed mild reversal of the albumin to globulin ratio with an increase in the beta fraction, presumably reflecting an increase in the beta lipoproteins. Serum urinalysis revealed glycosuria except for an occasional specimen which contained 10-30 mg of albumin per 100 ml. Other laboratory studies or findings which proved to be negative or within normal limits included blood cell counts, serologic tests for syphilis, blood urea nitrogen, glucose tolerance test, serum amylase, stool smear for undigested fat ( Sudan III), electrocardiogram, intravenous pyelogram, roentgenogram of the chest, a film of the abdomen. Bence Jones protein test, urinary concentration and dilution test, urine culture, Addison count, phenylsulfonphthalein test, and a battery of liver function tests. A lipid study was reported as showing no activity.

This patient's course at the hospital was uneventful. He demonstrated no hypertension. No definite cause was found for his mild intermittent albuminuria. He was placed on a rigid low fat diet (20 grams) and at the end of two weeks his total lipid dropped to 1500 mg per 100 ml and his blood cholesterol fell to 522 mg per 100 ml. The patient was then placed on a sitosterol preparation in doses of 1 tablet three times each day before meals. The patient's latest recorded blood cholesterol on this admission was 330 mg per 100 ml with 209 mg per 100 ml of cholesterol esters. Reported blood lipid studies were not reported by the day of discharge of this man. The patient's weight on discharge was 202 pounds. It was thought that his therapy was satisfactory and he was discharged to duty.

retirement When the patient was seen on an outpatient basis on 26 August 1957 he was asymptomatic and well He weighed 195 pounds His nonfasting serum was turbid but not milky His blood cholesterol was 296 per 100 ml with 224 mg per 100 ml as esters A pyridoxine unsaturated fatty acid preparation was added to his therapeutic regimen

### DISCUSSION

Essential hyperlipemia involves a defect in blood lipid regulation and any comments on this disease should include some remarks concerning the state of blood lipids and basic definitions The blood lipids include the triglycerides or neutral fats, the phospholipids, and cholesterol Most of the blood lipids are closely associated with the alpha and beta globulins in the form of lipoprotein complexes The so called beta lipoproteins are rich in fat and relatively low in protein and have been incriminated in the genesis of atherosclerosis The serum lipoproteins also have been characterized by ultracentrifugal techniques With this technic the rate of upward migration of a lipoprotein molecule under certain specific conditions has been expressed as Svedberg flotation units ( $S_f$ )<sup>1</sup> "An increase in the  $S_f$  number indicates an increase in the molecular lipid content, the size of the lipoprotein molecule, and a decrease in molecular density The major cholesterol and phospholipid bearing molecules are in the groups  $S_f$  17 and lower"<sup>1</sup> The  $S_f$  100  $S_f$  400 class and above to 40 000 are composed mainly of neutral fats and only small amounts of proteins, cholesterol, and phospholipids<sup>1</sup> A total cholesterol reflects the sum of the contributions of cholesterol from all members of the lipoprotein spectrum<sup>1</sup> It has been reported that the incidence of atherosclerosis is correlated with increases of certain classes of the lipoprotein spectrum

Although it has been suggested that the term "hyperlipemia" be used exclusively to indicate an increase in the neutral fat fraction of the blood lipids<sup>2</sup> it has become increasingly difficult to do so without qualification Following the example of Zilver smit<sup>10</sup> the term "hypertriglyceremia" has been used in this writing to indicate an increase in the blood neutral fats Hyper lipemia is utilized as a less specific term to indicate an increase in more than one fraction of the blood lipids with the implication that the blood neutral fats is one of these fractions Hypertriglyceremia is frequently associated with hyperlecithemia and hypercholesteremia though either of the latter two conditions may exist without an increase in the blood neutral fats<sup>11</sup> Alimentary hyperlipemia is a postabsorptive phenomenon in which an increase in the blood neutral fats follows a fatty meal The phospholipids and cholesterol may increase somewhat in the postabsorptive state though not to the same degree as the neutral fats and this is variable A sufficiently high concentration of neutral fat or very low density lipoprotein

molecules in aggregates or particulate form will render the blood serum milky white and impervious to light. This appearance of the serum is called lactescence and is known to occur in diabetic acidosis, nephrosis, acute pancreatitis, von Gierke's disease, and essential hyperlipemia.<sup>3</sup> Lactescent serum is not ordinarily found in diabetes mellitus, biliary obstruction, or hypothyroidism, although hypercholesteremia is frequently present in these diseases.

### Clinical Features

*Appearance of serum and lipoprotein pattern.* The case of essential hyperlipemia demonstrated the creamy white serum of extreme hypertriglyceremia. The patient was asymptomatic on admission. Ultracentrifugal lipoprotein studies were not done on his serum. Gofman and associates, however, demonstrated that patients with (as they termed it) essential hyperlipemia do have a distinctive lipoprotein pattern with a marked elevation of the  $S_f 20$ - $S_f 400$  classes which contain large amounts of neutral fats. Lever, Herbst, and Lyons also demonstrated these elevations and, in addition, found that two thirds of their patients with essential hyperlipemia had very large quantities of lipoproteins in the  $S_f 1^0$ - $S_f 20$  class.

*Family history.* Our patient's brother was said to have also had hyperlipemia, although it was not found in other members of the family. Lever and his group pointed out that it is impossible to really estimate the family incidence of this condition on the basis of the reports currently available. Many case reports contain no mention of the blood serum examination in relatives. In a review of 41 cases found in the literature, Lever, Smith, and Hurley<sup>3</sup> found evidence of elevated serum lipids in one or more relatives involving seven cases. Malmros, Swahn, and Truedson studied two patients with essential hyperlipemia and found similar conditions in four members of one family and one member of the other. A familial incidence has been reported in other cases in adults.

*Abdominal pain.* Recurrent noncharacteristic abdominal pain has long been observed as a particularly striking feature of essential hyperlipemia. It has been noted in about one half of the reported cases. The pain varies in location and nature and has been described as aching and colicky. It has been described as being so severe as to suggest an acute abdominal emergency. Sudden enlargement of the liver and spleen associated with an acute abdominal crisis was observed in one patient.

*Pancreatitis.* The diagnosis of acute pancreatitis has been adequately established in at least nine reported cases by elevation of the amylase in the serum or urine, or by exploratory laparotomy. It is probable that pancreatitis has been present in other cases which presented normal serum amylase values.

since this finding is not incompatible with the diagnosis.<sup>27</sup> Hypertriglyceremia has been observed in acute pancreatitis presumably as a secondary phenomenon.<sup>28</sup> It has been pointed out that marked similarities exist between the syndrome of relapsing pancreatitis with hyperlipemia and essential familial hyperlipemia with abdominal pain. Pancreatitis and hyperlipemia has been described in siblings. Both patients with relapsing pancreatitis and essential hyperlipemia have been reported to have other family members with asymptomatic hyperlipemia. Xanthomatosis, which usually indicates hyperlipemia, has been noted to appear before the onset of abdominal pain in some cases of relapsing pancreatitis and in some cases of essential hyperlipemia. Hepatosplenomegaly has been frequently reported in both diseases and the blood lipid patterns are the same. It has also been observed that patients with frank chronic pancreatic insufficiency fail to develop hyperlipemia. Klatskin and Gordon concluded from their studies that when chronic relapsing pancreatitis and hyperlipemia occur together, the pancreatitis is the result and not the cause of the hyperlipemia. This would seem to be true in our patient.

*Lipemia retinalis* Lipemia retinalis is a rare condition some times seen in hyperlipemic states. The vessels of the fundi are pale yellow or salmon pink in color, and described as ribbon like and flat. Because of the absence of an arteriolar light reflex, the differentiation of arterioles and veins must be made on size alone.<sup>29</sup> Joyner found nine cases of essential hyperlipemia in which lipemia retinalis was reported. Iolt<sup>31</sup> recently reported an additional case of lipemia retinalis in a child with essential hyperlipemia.

*Hepatosplenomegaly* Hepatosplenomegaly has been reported in almost all childhood cases of idiopathic hyperlipemia up to 1953. This feature previously had been noted in about one half of the cases in adults.<sup>7</sup> A review of the more recent literature reveals organ enlargement of one or the other type in less than one third of the adult cases. A diet which is low in fat has resulted in a decrease in the size of the liver and spleen in a considerable number of patients.

*Xanthomata* Lever, Smith, and Hurley<sup>3</sup> and Joyner<sup>7</sup> found descriptions of papular eruptive xanthomata in about one half of the reported cases of essential hyperlipemia. The lesions were described as yellow papules or nodules most commonly located on the extensor surfaces of the knees, elbows, buttocks, thighs and elsewhere. Many physicians have found that these lesions decrease or disappear on a low fat diet. Lever, Smith, and Hurley<sup>3</sup> stated that "Apparently there is no critical level for either neutral fat or cholesterol at which the xanthomatous lesions appear." Both Lever<sup>3</sup> and Malmros<sup>25</sup> and their associates found xanthoma tuberosum associated with essential hyperlipemia. It is likely that these conditions represent the same

or similar metabolic defects inasmuch as the ultracentrifugal lipoprotein pattern also is similar and patients with xanthoma tuberosum may have translucent serum. Gofman and his co-workers found striking differences in the serum lipoprotein pattern between cases of essential hyperlipemia and xanthoma tendinosum. Others<sup>1</sup> however have described xanthoma tendinosum in patients who ostensibly had essential hyperlipemia and it would seem reasonable at this time to conclude that the presence of any particular xanthomatous lesion should not make or preclude the diagnosis of essential hyperlipemia.

*Concomitant conditions* This diagnosis is ordinarily in compatible with the presence of nephrosis or diabetic acidosis. It is yet possible that essential hyperlipemia can exist concomitantly with other hyperlipemic states. Thannhauser<sup>2</sup> suggested that in the rare situation where creamy white serum has been found in the presence of hypothyroidism essential hyperlipemia is present. Hyperlipemia has been seen in severe untreated diabetes mellitus. This is completely reversible by adequate treatment of the diabetes but does not respond to a low fat diet.<sup>3</sup> Glycosuria and elevated blood sugars have been found in some patients with essential hyperlipemia. Joske and Adlersburg and Wang<sup>4</sup> reported cases of mild diabetes mellitus associated with idiopathic hyperlipemia. In these cases insulin was only effective in reducing the blood lipids to the basic levels of idiopathic hyperlipemia and the blood lipid levels remained above normal even on low fat diets. Lactescent serum occurs in a small proportion of patients with acute pancreatitis. The relationship of relapsing pancreatitis and essential hyperlipemia has been mentioned and is discussed thoroughly elsewhere. Adlersburg and Wang<sup>5</sup> suggested the possibility that diabetes mellitus and glycosuria in essential hyperlipemia frequently may be secondary to the relapsing pancreatitis found in this disease.

#### Prognosis and Treatment

The relationship of blood lipid abnormalities to atherosclerosis in essential hyperlipemia and other conditions is not fully understood. Increases in the blood cholesterol, the cholesterol to phospholipid ratio, the beta lipoproteins and the atherosclerogenic band of the lipoproteins have been studied in this respect with inconclusive results. It has been observed however that increases in the ultracentrifugal lipoprotein classes like those found in essential hyperlipemia may be associated with atherosclerosis.<sup>1, 2, 3</sup> About ten cases of essential hyperlipemia with adequate evidence of atherosclerotic heart disease have been noted in the literature since 1954. This number excludes those cases in which diabetes mellitus also was present. It is reasonable to conclude from the reports that essential hyperlipemia carries an un

favorable prognosis in terms of premature cardiovascular disease. A low fat diet may materially alter the abnormal blood lipid patterns and probably improve the prognosis. The strict adherence to low fat diet therefore is the most important therapy available to patients with essential hyperlipemia. Wilkinson<sup>22</sup> advocated the spaced fat feeding method of treating these patients in which no more than one fatty meal in any 24 hour period is allowed.

Sitosterol has been used with moderate success in one case of essential hyperlipemia.<sup>23</sup> Intravenously administered heparin has been found to produce a marked decrease in the blood lipids and also produce a significant change toward the normal in the ultracentrifugal lipoprotein pattern.<sup>21, 24</sup> Chlorpromazine has been reported to have a similar effect.<sup>24</sup> Neither of these agents is recommended for general long term use. Lecithin, choline, thyroxin, insulin, liver extract, pancreatic substance, and blood transfusions have been used in essential hyperlipemia with no noticeable effect.<sup>25</sup> The use of large doses of unsaturated fatty acids in the treatment of patients with this disease thus far has not been reported.

#### The Nature of Essential Hyperlipemia and Speculation

The exact nature of essential hyperlipemia remains obscure. Holt, Aylward, and Timbres<sup>26</sup> suggested that the hyperlipemia of this condition is due to the defective removal of the fat from the blood stream. Thannhauser<sup>2</sup> also classified this as retention hyperlipemia, similar to persistent alimentary hyperlipemia. Thannhauser and Stanley,<sup>3</sup> utilizing radioactive iodine techniques, suggested that idiopathic hyperlipemia is caused by decreased utilization of the fat by the tissue. Holt,<sup>26</sup> using similar methods, was unable to support this contention. Alimentary hyperlipemia can be abolished by heparin, but at present there is inadequate evidence that the absence of a clearing factor similar to heparin in the blood is the cause of idiopathic hyperlipemia.<sup>27</sup> Wilkinson<sup>22</sup> hypothesized that the sluggish removal of fat from the blood, hepatosplenomegaly, and abdominal crises are a reflection of a genetic homozygous abnormality in essential hyperlipemia. He further assumed that fat gradually accumulates in the blood over a long period because the lipids never quite return to the fasting level before a new fat meal is ingested.

Drigstedt and associates<sup>28</sup> made some interesting observations in experimental animals on the relationship of the pancreas to hyperlipemia. They indicated that although insulin treated, depancreatized dogs showed a profound fall in the serum lipids, dogs subjected to a subtotal pancreatectomy demonstrated a hyperlipemia and required considerably more insulin. In this second group of dogs with only a small portion of functioning pancreatic tissue, deviation of the pancreatic juice from the intestine reversed the hyperlipemia and need for additional

insulin Their work suggests that hyperlipemia may result from situations where adequate pancreatic juice allows fat absorption but inadequate pancreatic internal or endocrine secretion prevents regulation of the serum lipids It also was pointed out that alloxan treated dogs in which the beta cells are destroyed develop an insulin resistant diabetes although hyperlipemia is not present Inasmuch as the alpha cells are intact in these animals there has been some speculation on their ability to produce an internal secretion capable of controlling the blood lipids It has been reported that glucagon the hyperglycemic factor produced by the alpha cells reduces alimentary hyperlipemia and that destruction of the alpha cells is followed by a gradual increase in the serum lipids

The site of the fundamental lesion in essential hyperlipemia is not known but a substantial number of patients have demonstrated unequivocal evidence of pancreatitis Acute pancreatitis is known to cause hypertriglyceremia transient glycosuria and even diabetes mellitus The difficulty in establishing pancreatitis as an etiologic factor in essential hyperlipemia is that (1) excellent evidence is available that hypertriglyceremia has preceded overt evidence of pancreatic inflammation (2) chronic pancreatitis with frank pancreatic insufficiency is rarely if ever associated with hyperlipemia and (3) pancreatitis is not apparent in many cases of essential hyperlipemia On the other hand there is really little evidence to support the hypothesis that hypertriglyceremia can cause pancreatitis on the basis for instance of fat embolization Perhaps essential hyperlipemia is actually an inherited inflammatory disease of the pancreas which primarily involves the lipid regulating tissue to cause asymptomatic hyperlipemia and secondary effects If this were true then the appearance of abdominal pain and clinical pancreatitis would merely indicate exacerbation of a subclinical process already responsible for hypertriglyceremia and explain a perplexing time relationship in the association of pancreatitis and essential hyperlipemia This relationship remains an interesting problem in need of more thorough elucidation

#### SUMMARY

Hypertriglyceremia idiopathic and familial in nature is called essential hyperlipemia The fasting serum is usually milky white in this disease About seventy cases have been reported and another is presented The classical features of this disease include (1) opaque white serum in the fasting state (2) a family history (3) recurrent abdominal pain (4) lipemia retinalis (5) hepatosplenomegaly and (6) xanthoria of the skin The case reported was observed for an 11 year period

Recent reports indicate that essential hyperlipemia is associated with premature atherosclerosis and carries an unfavorable

prognosis A low fat diet is the best possible treatment for this disease and may improve the prognosis The nature of essential hyperlipemia is not known but the disease seems to be related to pancreatitis in some way This relationship is poorly understood, but there is some evidence that a lipid regulating tissue of the pancreas is injured in essential hyperlipemia, allowing abnormally high blood fat levels in the presence of normal fat absorption

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### SURGEON WITHOUT HANDS

The advent of anesthetic abolished the major need for excessive speed in operating and permitted a more deliberate and considered approach in contrast to the haphazard in flexible routine of the preanesthetic era. Anesthesia also made possible more complex operations which on the account alone were less likely to be performed repeatedly in a lavishly delicate way. A further step in the evolution of surgery away from a rigidly stylized mechanical craft was the application of basic science to everyday management of the surgical patient. Indeed, with the coming a long way toward the millennium envisaged by Harvey Cushing when he looked to the day that university authorities would appoint professional surgery man with no hands.

—C ROLLINS HANLON M D

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# HEARING LOSS FOLLOWING INADEQUATE TREATMENT OF OTITIS MEDIA

BYRON G McKIBBEN *Colonel MC USA*

THE use of therapeutic agents, developed during the past 20 years, has altered the clinical course of acute otitis media to such an extent that its more dangerous complications, such as acute mastoiditis, extradural and subdural abscess, lateral sinus thrombosis, suppurative meningitis and abscess of the brain, have become much less frequent<sup>1</sup> while a less dramatic, and frequently unrecognized, complication that of hearing loss, has become more common.

Prior to the introduction of the sulfa drugs, the treatment of acute otitis media was primarily a surgical problem. In that era myringotomy and evacuation of fluid from the middle ear was a common procedure. It was performed not only by the otolaryngologist but also by the general practitioner and by the pediatrician. With the relief of tension the pain subsided, the infection was cured and the hearing returned to normal. This procedure was performed early, in an effort to prevent bacterial invasion of the bony structures of the mastoid process and the petrous pyramid. The slogan of my pediatric professor was "strip that child and look at his ears" and it was not uncommon to do a myringotomy during the course of a physical examination. Simple mastoidectomy was a common procedure and it was considered to be as much of an emergency as appendectomy. While serous otitis media, frequently referred to as secretory otitis media, has been well known since 1867 when it was first observed and described by Politzer,<sup>2</sup> it was not considered to be a serious problem and some otolaryngologists apparently never recognized the condition until after the advent of chemotherapeutic and antibiotic drugs.

## INFLUENCE OF THE SULFA DRUGS

With the introduction of sulfanilamide and its various derivatives the management of middle ear infections became a combined medical and surgical effort. Sulfa drugs were administered, but myringotomy was still considered essential in the presence of a middle ear suppuration. With this combined medical and surgical management the course of the disease was influenced favorably and its dangerous sequelae were less commonly ob-

served Chronic middle ear effusion had not yet emerged as a serious threat to hearing acuity because incision and drainage of localized pus was still recognized as a surgical principle that could not be disregarded

### INFLUENCE OF THE ANTIBIOTICS

Shortly after the termination of World War II penicillin became available in large enough quantities to permit its use in many infectious processes. As the product was improved and its low toxicity became well known it was evident that the dosage could be greatly increased. This factor of low toxicity gave penicillin a great advantage over the sulfa drugs, large doses of which were precluded because of increased toxicity. Since the advent of penicillin many other antibiotics have been added to our armamentarium in the struggle against infectious diseases. The antibiotics have been so effective in the treatment of disease that it has been said that antibiotics have changed the face of medicine and that they have also changed the character of disease.

Penicillin when administered in adequate dosage early in the course of acute otitis media generally causes a prompt subsidence of pain. Acetylsalicylic acid and in some cases codeine may be required to relieve pain during the first 24 hours. Penicillin or one of the other antibiotics usually is given for a period of three to five days—in many instances this consists of a single intramuscular injection followed by a few days of penicillin by mouth. Because of the false impression that the patient is cured together with possible unfamiliarity with the difference in appearance between a normal tympanic membrane and a nearly normal one, further observation and treatment usually are not considered necessary. This of course represents unsound clinical judgment and leads one into a false sense of security.

One must not lose sight of the masking effect of these drugs. The infectious process may lie dormant or actually progress to a surgical condition in the mastoid or to a serious intracranial complication. Most of these sequelae occur in patients who have had inadequate antibiotic therapy, have not had a myringotomy and have not had adequate follow up observation. These sequelae may not be accompanied by alarming symptoms and may be difficult to diagnose.

Morrow deplored the practice of early abandonment of antibiotic treatment. He stated that it was known to be a frequent practice for acute otitis media to be treated by a single injection of penicillin with the matter of follow up observation being left to the discretion of the patient.

Many of these patients will recover completely. An alarming number, however, if examined with an otoscope will be found

to be in need of further treatment, and many of them will complain of impaired hearing in one or both ears. Otoscopic examination will reveal some abnormality in the appearance of the tympanic membrane. The type of abnormality will vary considerably, depending on the virulence of the infection, the sensitivity of the causative organism to the therapeutic agent, the dosage in which the drug is administered, and the natural immunity of the patient. The tympanic membrane may be light red or pink in color, the landmarks may be obliterated, and the luster may not have returned to normal, or it may be a dull gray with dilatation of the blood vessels on its surface, and the landmarks may just be returning. If the infection has been mild or the response to treatment was prompt, the drum may appear normal to the untrained eye, more careful observation, however, may reveal serous fluid in the middle ear. If considerable time has elapsed since the acute stage, any of the signs of serous otitis media may be observed. In this case the drum may present a salmon pink or amber color, and a fluid level or bubbles may be seen in the middle ear. This observation of course, makes the diagnosis easy. In the majority of cases, however, a fluid level or bubbles in the middle ear effusion will not be seen because the middle ear is completely filled, or because of a thickened or opaque tympanic membrane.

Hoople stated that "a full tympanum and, much more often than not the full mastoid as well, is ten times as prevalent as the ear which has only a (fluid) level line." He emphasized that the identifying feature is the over all amber color of the drum which may vary from a faint, barely perceptible yellowish tinge to a dark, bluish cast and that in the majority of these cases a helpful aid in making a diagnosis is the fact that the short process and handle of the malleus stand out as chalky white in contrast to the colored drum.

Walsh<sup>6</sup> stated that a creamy dull appearance to the drum is suggestive of a glue like mucoid exudate in the middle ear. Day<sup>7</sup> first applied the term "glue ear" to this condition some 25 years ago when it was called to his attention by his father. To become familiar with the appearance of the tympanic membrane in these cases, an otoscopic examination should be performed on all patients undergoing physical examination.

Davison,<sup>8</sup> Walsh,<sup>6</sup> and Day stressed the importance of the information to be gained by use of the pneumatic otoscope (figs 1 and 2). If there is fluid in the middle ear, the tympanic membrane moves poorly and the degree of immobility is in proportion to the amount of fluid in the middle ear. If the drum moves rapidly in response to rapid alteration in air pressure produced by the hand bulb there is little or no fluid in the middle ear. Walsh stated that an otologic examination that does not include use of the pneumatic otoscope is incomplete.

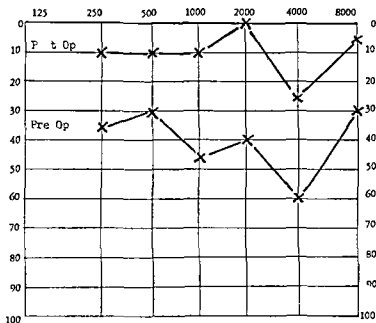


Fig 3 Left Pre-Op The w 38 d b l l th p b  
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The impression that acute otitis media is no longer a disease that requires surgical intervention has been widespread during the last 15 years. In 1953 Rutherford stated that the complacent acceptance of the antibiotics as a cure all in middle ear infections had resulted in a state where the younger pediatricians were unfamiliar with the technique of cleansing the ear canal that they were unable to observe and recognize the changes in the drum membrane which indicate pathologic processes in the middle ear and that they did not know how to perform a myringotomy. She further emphasized that some interns and residents were taught that myringotomy was a procedure to be avoided because it injured the tympanic membrane although spontaneous rupture under antibiotic therapy apparently was not considered to be harmful. She advocated the use of antibiotics in the treatment of acute otitis media only after myringotomy and general therapeutic measures have failed to effect a cure.

DeWeese commented that pediatric teaching was almost unanimous in emphasizing that myringotomy was unnecessary. He stated that it was unfortunate that students, interns, resi-

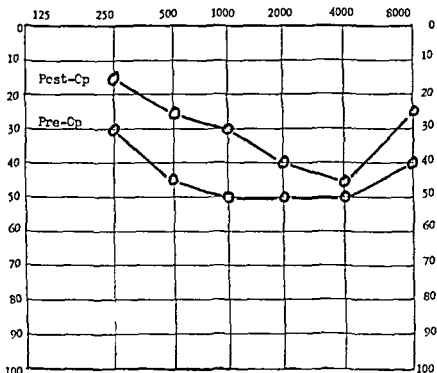


Figure 4 Right ear Pre Op There was 48-decibel loss in the speech frequencies prior to myringotomy Post Op After myringotomy the hearing was improved to the 31-decibel level—no definite line between good and bad hearing A small perforation in the posterior portion of Schrapnell's membrane (pars flaccida) discharging foul smelling exudate indicates chronic infection of the epitympanic space and mastoid and probably a cholesteatoma This accounts for failure of the hearing to return to normal after myringotomy and evacuation of serous fluid Modified radical mastoidectomy has been recommended for this ear

dents and even more unfortunate, that parents and other lay people had been told repeatedly that myringotomy is injurious to the drum membrane

The pediatrician<sup>4</sup> who discussed Rutherford's paper stated that if upper respiratory infections were properly treated, otitis media should be uncommon and that mastoiditis, chronic otorrhea, and deafness should be rare. He further stated that most of the cases of otitis media and its sequelae he had observed in one hospital occurred in the children who had had inadequate antibiotic therapy.

Rutherford stated that repeated attacks of acute secretory otitis media probably were the most common cause of chronic hearing loss and that in many instances these patients were being treated with antibiotics instead of measures to relieve the underlying cause—that of obstruction of the eustachian tube.

These cases require systemic decongestants such as ephedrine or Propadrine Hydrochloride (brand of phenylpropanolamine hydrochloride) vasoconstrictor nasal drops and in many cases a myringotomy. Restoration of tubal function may also require a carefully performed adenoidectomy and in some cases the treatment of some systemic condition such as allergy or endocrine imbalance. When a patient with this condition is treated without myringotomy sterile exudate may remain in the middle ear and lead to deafness. Antimicrobial drugs have no place in the management of serous (secretory) otitis media.

Dixon<sup>1</sup> recommended that when a patient with acute otitis media is first seen he be treated with crystalline penicillin 500 000 units intramuscularly twice daily for 5 days and that he be given vasoconstrictor nasal drops. If pain, fever or a bulging tympanic membrane persist for 24 hours after treatment is started myringotomy is performed but this is usually unnecessary. He stated that if after the acute stage has subsided there appears to be any residual fluid in the middle ear it should be removed by myringotomy. He stressed the necessity for follow up observation at regular intervals until the tympanic membrane appears normal and until audiometry shows that the hearing is restored.

### ANTIBIOTIC DEAFNESS

In 1949 Popper<sup>1</sup> first drew attention to a type of hearing loss which he termed antibiotic deafness and again in 1957 he described the condition stating that a more explanatory title would be antibiotic effusion deafness in order to distinguish it from deafness caused by streptomycin sulfate.

Popper stated that this type of deafness is the result of the great potency and large dosage of antibiotics and that the efficiency of these curative agents has become a menace to the function of hearing.

He observed 93 cases of antibiotic deafness over a five year period and stated that the diagnosis presented no difficulty. A typical history is that the patient had acute otitis media which responded promptly to antibiotic therapy the pain was relieved without aural discharge but hearing loss noted either by the patient or in the case of a child by the mother had not subsided. Otoscopic examination revealed that the tympanic membrane was not normal and myringotomy with evacuation of fluid from the middle ear was followed by return of hearing to normal. Repeat myringotomy was necessary in 25 of his cases and simple mastoidectomy was required in 18.

An interesting case was that of a farmer who was treated for severe earache with penicillin. The pain subsided within 24 hours without aural discharge but severe deafness persisted.

While on a hunting trip where no medical facilities were available, earache recurred. The tympanic membrane ruptured spontaneously with copious discharge and immediate improvement in hearing acuity. This man refused further treatment with penicillin because he feared it would cause the hearing loss to recur. He therefore was referred to Popper who convinced him that with adequate drainage he had nothing to fear.<sup>1</sup>

### PRESENT TREND

While there has been considerable difference of opinion as to when in the course of acute otitis media to start antibiotics and whether or not to perform a myringotomy, there is a growing tendency for physicians to agree on the importance of myringotomy in the management of this infectious process.

In 1953, DeWeese<sup>12</sup> stated that he believed there were signs of such a change in the pediatrician's attitude and Bigler<sup>1</sup> intimated that this would be a possibility if antibiotics could not keep pace with new types of bacterial infections or organism resistance.

In 1955, Silcox<sup>17</sup> commented that we have reached an era where infections of the ear and adjacent structures are not being controlled by antibiotics and that the complications of acute otitis media are being seen more frequently because of the development of antibiotic resistant strains of bacteria. He reported three cases of acute otitis media with rapid development of serious intracranial complications that were not controlled by antimicrobial drugs.

In 1956, Goodale<sup>18</sup> stated that the pendulum had begun to swing back toward the prechemotherapeutic era. He philosophized that we should have anticipated this as a typical biologic response that in time, all life makes an adjustment to its changing environment or becomes extinct. He called attention to the increasing tendency for microorganisms to develop resistance to antibiotics and mentioned the greater number of antibiotic resistant organisms, such as *Proteus vulgaris* and *Pseudomonas aeruginosa* that are being cultured from discharge from the middle ear. He further pointed out that patients frequently show allergic reactions to antibiotics and, therefore, are unable to be treated with them, even though the microorganisms responsible for their infection may be sensitive to the drug.

This increasing resistance of microorganisms to antibiotics induced Davison to employ massive doses of penicillin. He performed early myringotomy and evacuated the exudate with spot suction. This fluid, collected under sterile precautions, provides an excellent sample for culture and sensitivity studies.

Carp<sup>19</sup> stressed the importance of early myringotomy in cases of acute otitis media with a bulging tympanic membrane and



carache do stated that in the Pediatrics Department William Beaumont Army Hospital antibiotics (usually procaine penicillin 300 mg (300 000 units) daily and Terramycin (brand of oxytetracycline) 50 mg per kilogram of body weight up to 1 gram daily) are routinely prescribed for a period of 10 days. Follow up observation is continued until the tympanic membrane appears normal.

### SUMMARY AND CONCLUSIONS

The use of antimicrobial drugs in the treatment of acute otitis media has resulted in a marked decrease in the intracranial suppurative processes that may complicate middle ear infections. Coincident with this therapeutic achievement and because of the widespread impression that myringotomy and evacuation of middle ear fluid are no longer necessary there has been an alarming increase in the incidence of hearing loss resulting from retained serous or mucoid and even glue like exudate in the middle ear.

The emergence of strains of micro organisms showing an increasing resistance to antimicrobial drugs and resulting in an increasing incidence of failure to control acute otitis media and its complications has induced many physicians to give larger doses of antibiotics and has made them more aware of the importance of myringotomy. Despite this favorable trend in the management of acute otitis media far too many patients suffering from this condition are receiving inadequate antibiotic therapy and are being denied the benefit of myringotomy for the release of purulent exudate and for the alleviation of pain.

Before we can hope to see a decrease in the number of patients suffering from this type of hearing loss all physicians who treat acute otitis media must appreciate that a bulging drum accompanied by pain is sufficient indication for myringotomy and evacuation of middle ear exudate that an effective antibiotic should be administered in adequate dosage and that treatment should be continued until the drum appears normal and audiometric testing shows the hearing to be restored. These physicians must be familiar with the appearance of a normal tympanic membrane and they must be able to recognize the changes that indicate myringitis, nonsuppurative otitis media and suppurative otitis media. The findings in each case must guide them in their decision as to the treatment that is to be prescribed.

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### THE HAZARDS OF RADIATION

The hazards of radiation came dramatically into the news about 30 years ago when a number of women employed to paint luminous dials on watches were stricken with radium poisoning. The extraordinary developments of the atomic energy industry in recent years and the prospect of vast future growth pose many medical and public health problems. While it appears that the activities at the major Atomic Energy Commission installations have had a good safety record the growing use of radioactive isotopes in industrial plants laboratories hospitals and other places is increasing the number of people exposed to radiation hazard. Maximum protection needs to be given persons working with atomic substances and equipment. The permissible levels for radiation exposure set by government agencies can serve as a guide for the maintenance of safety among workers in this field.

# RHEUMATIC FEVER IN MILITARY PERSONNEL

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**R**HEUMATIC FEVER is a military problem of some magnitude. During World War II approximately 40,000 cases of the disease occurred in the combined Armed Forces. The disease ranked high as a noncombat cause of disability and loss of manpower. With prospects for a continuing large personnel in the Armed Forces, rheumatic fever will remain an important concern.

This report is based on a review of the records of 563 cases of rheumatic fever which occurred in military personnel during World War II. Four hundred and one patients with rheumatic fever were observed personally by one of us (E. P. E.) during World War II at an Army Rheumatic Fever Center (Torney General Hospital, Palm Springs, Calif.). Thirty-three of these patients and 102 additional patients who had rheumatic fever in World War II were observed in a follow-up study approximately six years after the attack of rheumatic fever in military service. Medical records were reviewed on 60 additional veterans in connection with the follow-up study, although these veterans were not examined in person.

At the time of this study, modified Jones criteria were used for diagnosis. As evidence of an attack of rheumatic fever, the patient must have had at least one major manifestation (carditis, self-limited arthritis, subcutaneous rheumatic nodules, or chorea) and at least two minor manifestations (fever, arthralgia, abnormal laboratory tests, epistaxis, or purpura, erythemas, including erythema marginatum, pneumonitis). Especially careful differential diagnosis was made to eliminate patients with rheumatoid arthritis, collagen disease, drug reactions, and other diseases which might mimic rheumatic fever.

## BACKGROUND DATA

The 401 patients admitted to Torney General Hospital, a special rheumatic fever center, were in all stages of their disease at the time of admission. Most patients were in a subacute

F m Vet      Admn      H p l P l Al      Cal f      d V      an Adm      tr  
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or convalescent stage of rheumatic fever, having been initially treated at nearby station or general hospitals. Rather complete medical records were available on these patients, though the type of clinical and laboratory studies, as well as treatment, varied somewhat during the period prior to their admission to the rheumatic fever center. The 162 patients not admitted to Tornev General Hospital were treated at nonspecialized general hospitals. No significant clinical differences were noted between this group and the Tornev group in regard to clinical manifestations of illness or outcome. Consequently it was believed that the group of patients studied was as nearly representative as any sample might be of patients with rheumatic fever in military service.

Approximately one half of the patients had their attack of rheumatic fever between the ages of 18 and 21 years. In 8 per cent rheumatic fever occurred in patients 34 years of age or older. Ninety four per cent of these patients were men reflecting the preponderance of men in the military service. Of the 563 patients, only 201 had a history indicative of an attack of rheumatic fever prior to military service, a prevalence of 35.7 per cent. History of "rheumatic fever," "inflammatory rheumatism," "Saint Vitus dance" or a "heart murmur" following a febrile illness were considered evidence of a previous attack. Two thirds of all patients had histories of tonsillitis or scarlet fever, suggesting previous streptococcal infection (table 1).

### CLINICAL FINDINGS

**Antecedent illness.** The clinical onset of rheumatic fever was preceded by a closely antecedent illness in 478 (85 per cent) of the 563 patients. In 443 of these patients the illness was described as a "cold," "acute nasopharyngitis," "acute tonsillitis" or "acute sinusitis." Twenty nine patients had scarlet fever, 3 had rubella and 3 had an attack of diarrhea. In 10 other patients episodes of unusual physical stress such as prolonged hikes or immersions preceded the appearance of rheumatic fever. Seventy five patients had no recognized incident prior to the attack of rheumatic fever.

The majority of patients in whom an antecedent infection occurred had a latent and relatively asymptomatic period of seven to twenty one days before the onset of acute rheumatic fever. When episodes of physical stress antedated the illness, symptoms of rheumatic fever occurred immediately thereafter.

**Arthralgia and Arthritis.** Arthralgia was present in 555 (98.6 per cent) of our 563 patients. Arthritis (objective changes in the joints) was present in 477 (85.3 per cent). The arthropathy involved many joints and was migratory in the majority of patients. It was usually the earliest clinical indication of rheumatic activity. Occasionally patients complained of vague

ns in their joints for days or weeks before the acute manifestations appeared. The latter however usually marked the onset of the disease with initial involvement of one of the weight bearing joints most commonly the knee or ankle. In 81 per cent of the patients the arthropathy was symmetrical and in approximately 50 per cent fingers and toes were involved. In 5 per cent of the patients only two joints were affected. Objective signs of joint disease were lacking in 14 per cent of the group. This factor helped to explain such early misdiagnoses as strain and flat feet.

TABLE 1 Clinical findings in 563 patients with rheumatism

History and physical examination	Number of patients	Percentage
Recurrent fever	201	35.7
Tooth infection	376	66.6
Antecedent illness	478	85.3
Initial signs		
Arthralgia	555	98.8
Arthritis	477	85.3
Carditis	231	41.0
Headache	114	20.3
Finger (99 Fingers)	518	92.0
Elvated tendons	552	98.2
Gonorrhea	450	80.0
Hemoglobin	104	18.4
Erythema	29	5.2
Purpura	28	4.9
Subcutaneous hemorrhages	8	1.4
Chills	2	0.4

Age group 22 years and under 42 years and over

Following the institution of maximum tolerated doses of salicylates objective manifestations in the joints usually appeared in less than 7 days. They never lasted longer than 4 weeks. Permanent objective changes in the joints as a result of rheumatic fever were not observed although some patients complained of prolonged arthralgia for many months after all signs of active disease had disappeared.

**Carditis.** Evidence of carditis was found in 231 of the 563 cases an incidence of 41 per cent. The signs of carditis in these patients are listed in detail in table 2.

Auscultatory signs of carditis were more frequent than electrocardiographic signs. The outstanding auscultatory sign was a systolic murmur. Systolic murmurs were graded for intensity (1 to 4) and were evaluated according to location, duration, transmission and quality. Grade 1 and Grade 2 systolic murmurs were considered to be of physiologic origin. Such murmurs usually transient were heard in 119 patients (21 per cent).

Various degrees of AV block and abnormalities of the ST segments and T waves were the most frequent electrocardiographic signs of carditis. Cardiac enlargement, pericarditis, and congestive heart failure were infrequent manifestations of carditis.

TABLE 2 Manifestations of carditis in 231 of 563 military patients with rheumatic fever

Manifestation of carditis	Number of patients	Percentage
Auscultatory	184	32.6
Systolic murmur Grade 3 or more	131	23.3
Diastolic murmur trace	29	5.1
Systolic and diastolic murmur mitral	16	2.8
Pericardial friction rub	21	3.7
Electrocardiographic	170	30.2
AV block (1st degree)	122	21.7
AV block (2nd degree)	13	2.3
AV block (3rd degree)	11	2.0
Abnormal ST & T waves	71	12.6
Bundle-branch block	1	0.2
Prolonged QT interval	4	0.8
Wandering baseline	10	1.8
Normal rhythm	6	1.0
Paroxysmal tachycardia	3	0.5
Fibrillatory baseline	1	0.2
Other diagnostic details	9	1.5
Cardiomegaly	9	1.5
Constrictive pericarditis	5	1.0

Residual signs of heart disease at the termination of an attack of rheumatic fever during military service were noted in 114 of the 563 patients in this series, an incidence of 20.3 per cent. Residual heart disease was determined by the presence of (1) cardiac enlargement, (2) diastolic heart murmurs, (3) electrocardiographic abnormalities, (4) systolic heart murmurs of Grade 3 or more even in the absence of cardiac enlargement. In 100 patients (17.7 per cent) the residual abnormality was manifested by significant heart murmurs. In 22 patients (3.9 per cent), electrocardiographic abnormalities remained. In 8 patients (1.4 per cent) cardiac enlargement was present at the end of the attack.

**Fever.** Fever was observed in 518 (92 per cent) of these patients. The median range of temperature elevation was 101 F to 102 F but in more than one fourth of the group the maximum oral temperature did not exceed 100°F. The temperature usually returned promptly to normal with recovery from a rheumatic cycle.

**Laboratory Tests.** The sedimentation rate was elevated at or shortly after the onset of the disease in over 98 per cent of the patients, and it was usually the last laboratory sign to return to normal. The average duration of elevation of sedimentation

rate was 11 weeks but in one third of the patients the elevation persisted beyond that time. Leukocytosis and anemia did not occur frequently enough to be considered as reliable signs of activity of the disease in themselves. Forty nine per cent of the patients had an elevation of the antistreptolysin titer to more than 333 Todd units but this test was not performed in every patient and not always early in the disease. Undoubtedly the frequency of elevated antistreptolysin titers would have been greater had this test been obtained constantly.

**Response to Salicylates.** The articular response to salicylates given in maximum tolerated dose was excellent in 80 per cent of these patients. In general objective changes in the joints disappeared within seven days after starting therapy. Frequently a recrudescence of arthritis occurred if salicylates were withdrawn prematurely. The effect of salicylates on the cardiac manifestations of rheumatic fever was not appreciable. A prompt and effective articular response to salicylates almost always constituted a fairly reliable diagnostic criterion for rheumatic fever. All these patients were treated prior to the clinical use of adrenocortical hormones in rheumatic fever.

**Additional Clinical Manifestations.** Epistaxis, purpura or petechiae were seen in 104 (18.4 per cent) of the 563 patients. Skin eruptions occurred in 99 (5 per cent). Erythema marginatum was observed in 10 patients, urticaria was found in 12 patients, and erythema nodosum in the remaining 7. Pneumonitis occurred in 28 patients. It was virtually impossible to differentiate rheumatic pneumonitis from so called primary atypical pneumonia which may have been the diagnosis in some cases. Subcutaneous rheumatic nodules were observed in only 8 patients. Chorea was also rare, occurring in only 9 of the patients. Both of these patients had a history of rheumatic fever in childhood.

## DISCUSSION

The epidemiologic factors of most importance in these patients were the presence of an antecedent infection and a past history of rheumatic fever. Antecedent infections were recorded in 85 per cent of our cases, which is similar to the incidence of 75 per cent more recently recorded. While the presence of an antecedent infection is no guarantee of rheumatic fever, its absence should demand strong additional support for the diagnosis. The prevalence of a past history of rheumatic fever varies greatly in adults with the disease, ranging from 5 to 54 per cent. However, it appears that more than one quarter of all patients have previously had rheumatic fever. The presence of such a history increases the likelihood of a rheumatic recurrence while its absence does not mitigate against the diagnosis.

Evidence of carditis and a self limiting polyarthrits responding well to salicylates were the most important clinical signs of rheumatic fever. Subcutaneous nodules, chorea and erythema marginatum were rare manifestations of the disease at this age, and in none of our cases occurred without arthritis or carditis. In adults arthritis is much more frequent than carditis at least twice as often in these patients. More than three-quarters of patients with significant carditis were diagnosable by auscultatory signs. However in a number of patients, electrocardiographic abnormalities were the sole evidence of carditis. Only 7 of the 563 patients were diagnosed as having rheumatic fever in the absence of signs or symptoms of joint disease. In 9 other patients the signs of carditis preceded those of arthritis in one instance by as much as 4 months. Several studies have disclosed that carditis without or preceding arthritis may occur in adults with rheumatic fever.<sup>5</sup>

A frequent problem in the diagnosis of carditis is the proper evaluation of systolic murmurs usually apical which are not easily heard. When such murmurs occur without other evidence of heart disease even during the acute stage of rheumatic fever it is doubtful that they should be considered as indicative of carditis. A follow up study of veterans with rheumatic fever in World War II provided a particularly good retrospective analysis of such murmurs.<sup>2</sup> Although such systolic murmurs were heard in 46 of 130 patients during the adult rheumatic attack only one had a murmur considered significant when observed 4 to 8 years later. Twenty five still had a Grade 1 systolic murmur while 20 no longer had audible murmurs. This experience leads us to conclude that heart murmurs which would be considered physiologic probably are even in the presence of acute rheumatic fever.

Personal heart disease was found in 20.3 per cent of the patients in this study, a prevalence comparable to that observed by others.<sup>7-9</sup> This low prevalence of cardiac affection is below that reported for children. It should be remembered that it does not reflect any effect from treatment with corticosteroids. Considerable prognostic significance can be attached to the fact that the heart usually remains unchanged for several years after an attack of rheumatic fever in adult life.

Since World War II the diagnostic criteria for rheumatic fever have been changed.<sup>1</sup> Major manifestations now include carditis, polyarthrits, chorea, subcutaneous nodules and erythema marginatum. Minor criteria include fever, arthralgia, atrioventricular block, abnormal laboratory tests (increased ESR, WBC, or presence of C-reactive protein), preceding beta hemolytic streptococcal infection or previous history of rheumatic fever. A diagnosis of rheumatic fever requires the presence of at least two major criteria or the combination of one major and two minor criteria. Even with the revised criteria the cases in this study



would still have been diagnosed as rheumatic fever. However, a considerable number would have been so diagnosed on the basis of the weakest combination possible (polyarthritides fever and elevated ESR). The relative rarity in military personnel of three major criteria (chorea, subcutaneous nodules and erythema marginatum) and the difficulty in definitely proving preceding streptococcal infection (unavailability or oversight in obtaining throat cultures or antistreptolysin titers) reduces the number of usable diagnostic criteria. In such cases, a presumptive antecedent streptococcal infection or a past history of rheumatic fever may add to the security of the diagnosis.

The long period during which military patients are customarily observed during such an illness tends to eliminate other confounding diseases such as collagen diseases, bacterial endocarditis, leukemia, sickle cell anemia, tuberculosis, poliomyelitis and infectious mononucleosis. Most difficulty in diagnosis arises in distinguishing between rheumatoid arthritis and rheumatic fever. The presence of an antecedent infection or a self-limiting course with a good response to salicylates favors rheumatic fever but is not entirely reliable. The new serologic tests for rheumatoid factor are not likely to be helpful in the differential diagnosis early in the course. Persistent arthralgia even after all other clinical evidences of rheumatic activity have subsided may add to the confusion. Post-rheumatic arthralgia lasting as long as six years following a rheumatic attack in military service was found in two thirds of the patients seen in our follow-up study.<sup>2</sup> In no case were objective changes found in the affected joints to support a diagnosis of rheumatoid arthritis.

#### SUMMARY

The clinical aspects of rheumatic fever in military personnel were reviewed in 563 cases occurring during World War II.

A previous history of rheumatic fever was discovered in slightly more than one third of the patients. Previous histories suggesting streptococcal infection were found in two thirds of patients. A closely antecedent illness occurred in 85 per cent of cases. Younger adults, usually below the age of 21 years, were most frequently affected.

Polyarthritides, which occurred in 85 per cent of patients, was the most important clinical manifestation. Characteristically, it was self-limiting, responding to salicylate therapy. Carditis manifested in most cases by the presence of pathologic heart murmurs was found in only 41 per cent of patients. In some patients, the only manifestations of cardiac involvement were electrocardiographic abnormalities, mainly atrioventricular block and ST-T abnormalities. Other common clinical findings were fever, arthralgia and elevated sedimentation rate. Erythema

marginatum, subcutaneous nodules and chorea were rare in these patients. For this reason a previous history of rheumatic fever, a well documented antecedent streptococcal infection, or atrio ventricular block may be more reliable diagnostic criteria in adult patients.

Residual heart disease following rheumatic fever was present in 20 per cent of these patients. Such heart disease was manifested by a pathologic heart murmur in most cases. This favorable outcome was obtained prior to the use of corticosteroids.

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# MEDICAL AMBASSADORS

Physicians as a group have a better record in military service than does any that I can think of chiefly because of the Doctor Draft Law. There are many among you who know whereof I speak. But there are also many and increasingly more young physicians who have not had this experience. More is the pity because medicine speaks a universal language and the physician is in consequence the best ambassador of goodwill. There are many outlets in foreign lands through which any number of our young physicians could find such experience. Let me cite only a single small but very important one there ought to be an American physician in every American Embassy of the world. Yet today not half a dozen physicians are so stationed.

—RICHARD A. KERN, M. D.  
in *Annals of Internal Medicine*  
pp 238-239 Aug 1958

# CARCINOMA OF THE CERVIX

Incidence in Relation to Clinical Findings

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**E**XFOLIATIVE CYTOLOGY of the female genital tract has become firmly established as an effective means of cancer detection and the literature on the subject is extensive. While there is no argument over the value of the cytologic screening procedures, the results concerning the numbers and percentages of positive smears and subsequently detected malignancies as reported from different medical centers vary considerably. The reported incidence of carcinoma of the cervix ranges from as low as 2.5 to as high as 11.8 per 1,000 women examined. These findings are influenced by the type of the particular segment of population examined, by the use of the cytologic examination as a screening or as a selective diagnostic procedure, and by the histologic criteria used for arriving at a diagnosis of carcinoma in situ. The uncertainty surrounding the microscopic diagnosis of carcinoma in situ makes an evaluation and comparison of series of examinations difficult. This applies to the reported incidence of carcinoma as well as to the reported accuracy of the cytologic diagnosis. Liberal criteria in the microscopic diagnosis of carcinoma in situ obviously reduce the percentage of false positive cytologic diagnoses.

This study was undertaken in order to determine the incidence, respectively the rate of detection, of carcinoma of the cervix in our own material. The population group examined is unique, most of the women being wives of service personnel or female service personnel, and the average age of this group is younger than that in most comparable series. At the same time we tried to determine the incidence of pelvic malignant disease in relation to the symptoms and to the clinical appearance of the patients.

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## MATERIAL AND METHODS

During the period from 1 February 1953 to 10 April 1958, cervical and vaginal smears from 8465 patients were examined at this laboratory. These cases were submitted from station hospitals, dispensaries, and other Armed Forces medical facilities throughout the Fifth U. S. Army Area, which includes 13 states. Most of the patients were dependents of service personnel, but there were also many female members of the armed services. The great majority of the smears was taken as a routine screening procedure. In tabulating these results, the patients were grouped according to the clinical history and the physical findings in order to determine whether detected lesions could be correlated with the clinical appearance. Criteria used for placing the patient in the different groups, the total numbers of patients, and their average age are shown in table 1. In instances where there were both symptoms and physical findings, the patients were placed according to the latter.

TABLE 1 *Criteria used and average age of five groups of patients studied*

Group	Criteria	Number of patients	Average age (years)
I	Routine mass No symptoms Clean cervix	5210	37
II	Physical finding described abnormal polypoid erosion granularity leukoplakia cysts	1515	34
III	Symptoms described vaginal discharge vaginal potting chronic cervicitis menstrual irregularity contact bleeding	1311	35
IV	Dependent patient	349	26
V	Carcinoma of the cervix previously diagnosed and treated in the past by radiation or hysterectomy	80	38

The cases were classified and reported as groups I through V, the criteria being those given by Papanicolaou. For practical purposes, groups III, IV, and V were regarded as being positive and additional smears or biopsies were recommended.

Table 2 shows the total numbers as well as the percentages of positive smears for patients in the groups defined above. Also shown are all cases of atypical squamous hyperplasia, atypical squamous metaplasia, and leukoplakia combined under the heading, Atypia. The cases of carcinoma in situ and invasive carcinoma. Our criteria for a diagnosis of carcinoma

TABLE 2 Cyt log / d g 8 465 pat ent

G p	N mb p t	P t m		Diag		
		Numb	P nt	A yp	C m	I ar m
I	5 210	26	0 5	7	4	1
II	1 515	39	2 6	6	4	2
III	1 311	34	2 6	2	4	0
IV	349	2	0 6	0	0	0
V	80	3	3 8	0	0	0
T t l	8 465	104	1 2	15	12	3

A yp 1 quam us hype pla typ 1 quam us met pl d l k pl k

in situ are strict and some of our cases of atypical squamous metaplasia or atypical hyperplasia could be classified as carcinoma in situ if more liberal criteria were used

The total numbers and percentages of carcinoma in situ and invasive carcinoma discovered in each group are given in table 3

TABLE 3 I cid / m 8 65 p t t

G p	N mb f p t t	Numb w h f p ar m	R p 1 000
I	5 210	5	1
II	1 515	6	4
III	1 311	4	3
IV	349	0	0
V	80	0	0
T t l	8 465	15	1 8

### DISCUSSION

The number of cases of carcinoma found per 1 000 patients examined is lower in our series than in most reports. The fact that strict criteria for a diagnosis of carcinoma in situ were used probably contributed to these results but we believe that the more important factors were the relatively low average age of our patients and a relatively high percentage of single female service personnel in the series. While the percentage of cases of carcinoma detected per positive smears is essentially the same in the different groups there is a significant difference

in the incidence of carcinoma for the total number of patients examined in each group. Of the over 5,000 women in group I, with an average age of 37 years who had no symptom and who had a completely normal appearing cervix, the incidence of carcinoma of the cervix was only 1 per 1,000. On the other hand, in both groups II and III, consisting of the women with either symptoms or positive clinical findings, the incidence of carcinoma of the cervix was between 3 and 4 per 1,000. The number of detected carcinomas in each group was small, but it is to be noted that in close correlation to the cases of carcinoma, the number of positive smears is similarly approximately five times greater for groups II and III than for group I. No carcinomas were found in follow up examinations after treatment or in pregnant women, but too few patients were in these groups to make the findings significant. From these results one may conclude that, while cytologic examinations are a most valuable screening procedure, the chances of finding suspicious or malignant cells on smears and of discovering a carcinoma are approximately three to four times greater in patients who have either symptoms or physical findings related to the genital tract.

#### SUMMARY

The results of cytologic examinations of the female genital tract on 8,465 women are reported. The incidence of carcinoma of the cervix was found to be 1 per 1,000 in patients with a negative history and no remarkable physical findings at the time the smears were taken. The incidence was between 3 and 4 per 1,000 in patients with positive physical findings or a history of symptoms related to the genital tract. The over all low incidence of carcinoma as compared to other surveys is attributed to the select nature of the group examined. The history and the physical findings certainly should not be used to determine which patient should be examined by cytologic methods, but a higher incidence of positive findings can be expected if there are symptoms or if there are visible lesions in the cervix.

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# PERICARDIAL CYSTS AND DIVERTICULA

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**P**ERICARDIAL CYSTS and diverticula are benign relatively rare structures that seldom produce symptoms or cause signs detectable by physical examination X-ray studies of the chest including fluoroscopy tomography and use of induced pneumoperitoneum may enable the discovery delineation and localization of an abnormal structure in the vicinity of the pericardium but do not provide an accurate differentiation of a cyst or diverticulum from a malignant neoplasm It is chiefly this difficulty of establishing an accurate diagnosis that has stimulated continuing surgical interest in these lesions Five cases treated surgically during the past eight years are presented below

## CASE REPORTS

**C 1** A 31 year old warrant officer developed cough fever and malaise Under treatment with bed rest and penicillin his symptoms subsided completely within a few days Serial roentgenograms of the chest however revealed a persistent density just above the left border of the cardiac shadow Fluoroscopy located this lesion anteriorly The structure transmitted pulsation of the heart Result of physical examination and routine laboratory studies were normal A left thoracotomy was performed through the fifth intercostal space and a thin walled translucent cyst 4 by 3 by 3 cm attached by a fibrous pedicle to the pericardium anterior to the phrenic nerve was excised and opened into the pericardial sac The excised lesion was a unilocular cyst containing a yellowish cloudy fluid The wall was thin and fibrous with a lining of flattened epithelial like cells Scattered collection of lymphocytes were found in the wall The postoperative course was uneventful and the patient was restored to full duty

**C 2** A 25 year old man was asymptomatic but a routine roentgenogram of the chest disclosed a density adjacent to the right cardiac border just above the diaphragm Further roentgenograms including a study using induced pneumoperitoneum more clearly delineated the mass and localized it anteriorly (fig 1 and 2) Result of physical



*Figure 1 (case 2) Post roentgenogram of chest roentgenogram with induced pneumoperitoneum demonstrating mass in right caudophrenic angle*

examination and routine laboratory studies were essentially normal. An upper gastrointestinal series of roentgenograms, barium enema roentgenograms and intravenous urography were normal. Bronchoscopy was negative. A thoracotomy was performed with subperiosteal resection of the sixth right rib. The lesion was found to be a thin-walled cyst attached to the pericardium. No continuity of the cyst lumen with the pericardial sac was found. The cyst was excised without difficulty. It was 6 by 5 by 3 cm in size with a thin translucent wall and was filled with serous fluid. The inner surface of the wall was bright shining white with irregular trabeculations and overlapping of the membranes giving a multilocular appearance. On microscopic study the wall was found to be composed of edematous collagenous connective tissue and fat with a lining of flat mesothelial cells. The postoperative course was uncomplicated and the patient returned to full duty.





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C 3. A 21 ye r-old man came to medical tention b ause of an acute respir tory inf ct on which subsided p omptly with symptomatic therapy S al ro ntgenogr ms of the ch st however revealed a per sistent m ss in the left cardophrenic angle Furthe r entgenograms localiz d the mass anteriorly Results of physical xamin tion nd out ne l boratory studies were essentially normal Thro gh a l ft thoracotomy thin walled cy t t tach d to the pe cardium was excis d I th c e th re d d app ar to be communic tion of the cyst lume thro gh the pedicle with the pericardi l ac The ma s was 2.5 by 2 by 7.5 cm Its wall w s 0.1 cm thick The structure was unilocula with mooth glistening lining that var d from pink t gray pink Microsc p study showed the lining to be layer of fl t ed eph l l cells The w ll was hyalinized connective fib us tissue which wa nfilter ted in some are s by ro d cells Th post p rative rec v ry was un v ntful The p tient eturned to full d ty

**Case 4** A 20 year-old man was hospitalized because of an abnormality seen in a routine chest roentgenogram. He had no complaints and the physical examination was essentially normal. All laboratory studies were within a normal range. Roentgenographic studies of the chest demonstrated a globular lesion at the right cardiophrenic angle not sharply defined but measuring roughly 3 by 4 cm. Lateral films localized this lesion anteriorly. Tomography did not add to this information. An upper gastrointestinal roentgenographic series and barium enema roentgenograms were essentially normal. At operation through a right thoracotomy a translucent cyst 2 by 3 cm was encountered at the pericardium adjacent to the crossing of the phrenic nerve. The cyst was removed with ease and detached from a thin fibrous stalk which was attached to the pericardium. Patency of this stalk could not be determined. The cyst was unilocular. The postoperative course was uneventful and the patient was returned to full duty.

**Case 5** A 23 year old first class petty officer was discovered by routine chest roentgenography to have a density at the right cardiophrenic angle. For several years he had had a slight cough in the mornings. It was productive of only a few ml of mucoid sputum daily. Physical examination was negative. Routine laboratory studies were all within normal limits. Multiple roentgenographic studies of the chest including tomography and the use of induced pneumoperitoneum further delineated and localized the lesion anteriorly at the right costo-phrenic angle (figs 3 and 4). Some of the films suggested the possibility that the lesion was a hernia through a foramen of Morgagni. An upper gastrointestinal series of roentgenograms and a barium enema study were normal however. Thoracotomy through the right sixth intercostal space revealed the lesion to be a thin walled translucent diverticulum of the pericardium. This structure 5 by 4 by 4 cm was attached to the pericardium by a narrow stalk through which there was free communication with the pericardial sac. Pressure on the diverticulum would empty its fluid contents into the pericardial sac. The diverticulum was easily excised. It was a unilocular cystic lesion with a thin fibrous wall lined by a single layer of flattened epithelial like cells (fig 5). The postoperative recovery was uncomplicated and the patient returned to full duty.

## DISCUSSION

Since 1934, when Pickhardt<sup>1</sup> reported the first successful surgical excision of a cyst adjacent to the pericardium, several small series of such cases have been reported. Blades,<sup>2</sup> in 1946, reported 10 pericardial cysts as part of a series of 109 mediastinal tumors collected from five U S Army hospitals during World War II. Bradford, Mahon, and Grow<sup>3</sup> reported eight cases in 1947. Drash and Hyer,<sup>4</sup> in 1950, reported five cases from the University of Virginia, and discussed 16 others from the literature. Lillie, McDonald and Clagott reported 12 cases from the files of the Mayo Clinic, and reviewed 25 others collected from the literature.



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up to 1950 Davis Dorsey and Scanlon reported two cases in 1953 Other similar reports are to be found in the literature <sup>7-1</sup>

In many instances these lesions have been asymptomatic In some cases however patients had cough dyspnea pleuritic type of pain, substernal pain a sense of precordial pressure tachycardia or flutterin<sub>g</sub> of the heart It seems reasonable that the local pressure of a large cyst might cause such symptoms

Characteristically these lesions are thin walled cystic structures Usually they are unilocular The wall is composed of fibrous connective tissue lined by a single layer of flattened cells resembling serosal or endothelial cells The cysts usually contain a clear colorless or yellowish fluid with physical and chemical properties suggestive of a transudate These lesions are most common in one of the cardiophrenic angles adjacent to the anterior chest wall more of them occur in the right cardio



*Figure 4 (case 5) Right lateral chest film with indicated pneumoperitoneum delineating mass anteriorly in right costophrenic angle*

phrenic angle than in the left one. However, they can occur elsewhere in the mediastinum, adjacent to the pericardium.

The origin and precise nature of these cystic structures is obscure. A widely accepted theory of their origin is that advanced by Lambert,<sup>7</sup> who stated that in the development of the pericardium, in embryonic life, a series of disconnected lacunae appear in the mesenchyme. These enlarge, gradually merge and form the pericardial coelom. Failure of one of these lacunae to merge with the others results in cyst formation. Other possible developmental sources of a cyst in the vicinity of the pericardium are (1) a pinched off fold of pericardium, (2) a pinched off fold of pleura, and (3) a lymphogenous cyst. Actually, it seems probable that several types of cystic lesions may exist in the vicinity of the pericardium. Lymphogenous cysts (cystic hygromas) may be differentiated by a tendency to a multilocular character, by the presence of elastic tissue and smooth muscle in the cyst.



Fig 5 (a 5) Photomicrograph of wall of diverticulum containing dilated lymphatic channels ( $\times 700$ )

wall and by the frequent association of smaller dilated lymphatic channels. Maier has reported pericardial diverticula that appeared to be of acquired origin presumably the result of increased pressure within the pericardial sac during a pericardial effusion.

The establishment of an accurate diagnosis is of great practical importance. Thyroid cysts and tumors, teratomas, lipomas, and paraesophageal cysts can mimic the roentgenographic appearance of a pericardial cyst. Also, it may be difficult by roentgenographic studies to differentiate a hernia through a foramen of Morgagni from a pericardial cyst. In the final analysis, surgical exploration is required to establish the diagnosis with certainty.

#### SUMMARY

Three pericardial cysts and two pericardial diverticula, all of which were discovered by roentgenograms of the chest, are reported. The differential diagnosis includes several types of mediastinal cysts and tumors, some of which may be malignant, and a hernia through a foramen of Morgagni. Because of the necessity of ruling out a malignant lesion, the therapy of pericardial cysts and diverticula requires surgical exploration and excision.

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## CURATIVE EFFECT OF CLAIMS SETTLEMENTS

One hundred patients with previously diagnosed cervical neck strain following auto accidents whose litigation on compensation claims had been settled were queried as to their present clinical status. After legal claims for damage were completed 88 per cent showed recovery and over half of these had no residual complaints. Many emotional factors but especially those concerning monetary compensation greatly confuse proper medical evaluation and appear to be the cause of the wide divergence of professional prognostic opinions relative to this particular injury.

—NICHOLAS GOTTEN M D

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# THE PARTIAL MASKING OF ANEMIA BY CONTRACTED BLOOD VOLUME

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**A**NEMIA is often suspected from a patient's appearance and confirmed by measuring the concentration of hemoglobin in his blood. The hemoglobin values of normal people are usually between 12 and 16 grams per 100 ml of blood, the hematocrit 40 to 50 per cent, and anemia is often defined as the state in which the hemoglobin or hematocrit is lower than normal. Now methods are available for measuring the size of the mass of circulating red blood cells, and we are learning to define anemia in terms of milliliters of red cells per kilogram of body weight. Total mass of circulating red blood cells in normal people is usually between 26 and 31 ml per kg of body weight. Women have less red cells per kg than men, and because adipose tissue is poor in blood, obese people have fewer red cells than thin ones.

These interesting studies have revealed that the concentration of hemoglobin in the blood is not always a true index of the total amount of hemoglobin. It is well known that, for example, after a severe hemorrhage the blood volume may be reduced by one or two liters, but for a time the concentration of hemoglobin remains unchanged. Less obvious examples of a lack of correlation have been demonstrated in pregnancy, where it has been shown that the "physiological anemia of pregnancy" may be due to an increase of plasma volume rather than a reduction of red cells. The same hemodilution may occur in advanced cirrhosis. In polycythemia vera the total blood volume is expanded as well as the red cell volume. The total red cell mass may be more than doubled (e.g., from 30 ml per kg of body weight, it may increase to 75 ml), but the hematocrit in the same patient may increase by only one half. From 45, the hematocrit may increase to 70 per cent.

This article calls attention to one of the consequences of severe anemia on the blood volume, and the clinical significance of this phenomenon is commented on.

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F m W l R d A m y I f R b W l e r R d A m y M d I C e r  
W h g t D C

## MATERIALS AND METHODS

The study involved measurement of the red blood cell mass and the venous hematocrit of a number of normal subjects and patients with severe anemia. Thirty four soldiers, participating in various transfusion studies in this department, comprised the control group. All were in good health with normal habitus. Thirty one patients included in the study were among those admitted to the hematology service of Walter Reed Army Hospital. We have not included any patients who were pregnant or suffering from cirrhosis, or malignant disease with cachexia. The diagnoses are shown in figure 1.

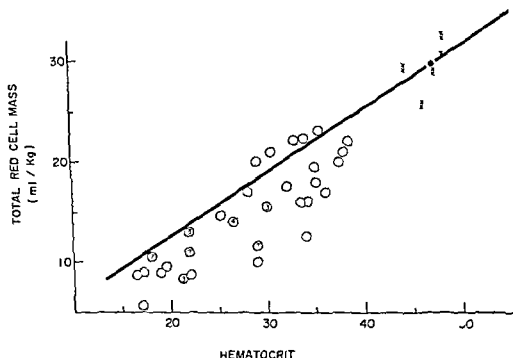


Figure 1 The partial masking of anemia by reduction of the total blood volume. The solid dot represents the average hematocrit (46.8 per cent) and the average red blood cell mass (29.7 per cent) of 34 normal subjects. The averages were divided one into the other to determine that every hematocrit point represents 0.635 ml per kg of circulating red cells. Using this value the line was drawn to demonstrate the corresponding volume of red cells for every hematocrit value. The line also represents values for hematocrit and red cell volume that would be obtained when the total blood volume remains constant and a quantity of plasma substitutes for an equal quantity of red cells. Notice that in every case of severe anemia the point falls below this line. This indicates that the total blood volume is diminished below the plasma and does not expand sufficiently to compensate directly for the reduction of the red cell mass. The distance of any point from the line is a measure of the amount by which the hematocrit value falls in spite of the reduction of the red cell mass. The patients are listed in table 1, group indicated by an enclosed number: (1) iron deficiency anemia, (2) pernici- ( ) pernicious anemia, (3) aplastic and refractory anemia, (4) bone marrow anemia including splenectomized cases, (5) acute hemolytic anemia, (6) acute hemolytic anemia, and (7) chronic hemolytic anemia.



Red blood cell mass was measured by the transfusion of a measured volume of red cells tagged with radioactive chromium (Cr). The red cell mass was computed by determining the extent to which the Cr was diluted after it had mixed with the entire amount of circulating blood. The values are stated in terms of milliliters of circulating red cells per kilogram of body weight.

The hematocrit was measured in capillary tubes spun on a high speed centrifuge. The values are stated in terms of packed red cells to the per cent of whole blood or as ml per 100 ml.

## RESULTS

The 34 normal subjects were found to have an average hematocrit of 46.8 with a range from 41 to 50. Their red cell mass averaged 29.7 ml per kg of body weight with a range from 25.5 to 35 ml. The distribution is shown in figure 1. The averages indicate that there were 0.6 ml of circulating red cells for every hematocrit point. Using this value a line was drawn on figure 1 representing the corresponding value of circulating red cell mass for every hematocrit point between 15 and 55.

The 31 patients represented in figure 1 were those with a red cell mass less than 2 ml per kg. The average red cell mass of the group was 14.9 ml with a range from 5.4 ml to 22.5 ml per kg. The average hematocrit was 28.3 with a range from 16.5 to 38.5. The wide scatter of the values around the average is shown in figure 1 where each patient is represented by a number referring to his diagnosis. When we treat the averages as we did those of the normal group it is found that there are 0.5 ml of circulating red cells for every hematocrit point, a deviation from the normal average amounting to 17 per cent. The hematocrits of the anemic patient indicate anemia of less severity than do the corresponding values for the red cell mass. When plotted on the graph in figure 1 the points lie below the line which represents the normal relationship of hematocrit to red cell mass (0.6 ml of red cells for every hematocrit point). This abnormality is sometimes called "hemoconcentration."

To demonstrate what happens to the blood and red cell volumes in severe anemia let us select some arbitrary value as an example. Consider a hypothetical healthy man whose total blood volume is 70 ml per kg of body weight, of which the red cell mass is 30 ml and plasma volume is 40 ml. His venous hematocrit is 48 per cent. This hypothetical man develops

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aplastic anemia and, when we measure his blood volume again, the red cell mass is 10 ml the plasma volume 50 ml, and the total blood volume 60 ml per kg. The plasma volume has increased to compensate for the loss of red cells, but it has not increased enough to provide a total blood volume equal to the initial 70 ml. The venous hematocrit is now 24. The total red cell mass is decreased by two-thirds but the hematocrit is decreased by only one-half. In terms of circulating red blood cells per hematocrit point, the initial value is 0.6 ml the value after anemia develops is 0.4 ml. The values of the patients in figure 1 values as low as 0.4 ml were

#### Partial Masking of Anemia

# AIR FLOW OBSTRUCTION IN ALLERGIC ASTHMA AND ITS EFFECT ON THE LUNG COMPARTMENTS

An Analysis of Lung Compartment Relationships in 42 Cases

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**O**BSTRUCTION to air flow within the bronchial tree has been designated as the principal abnormality in the pathogenesis of obstructive emphysema. The anatomic counterpart of the functional air flow impairment is bronchial obstruction or bronchospasm or both. Spain and Kaufman<sup>1</sup> reported on the histopathology of the lung in emphysema and described in detail the anatomic changes which obstruct the lumens of the terminal and respiratory bronchioles. Whether or not bronchospasm forms a physical basis for air flow obstruction will not be discussed in this report. Suffice it to mention that some authors believe that at the present there is no factual evidence for the existence of bronchospasm in the bronchial tree.

The proponents of bronchiolar obstruction further contend that air flow impairment by establishing a state of air trapping produces hyperinflation of the alveoli which eventually leads to mechanical overdistension of the lungs. The distended alveoli effect an impairment in the blood and oxygen supply which produces further advances in the degenerative changes of tissue atrophy and disruption. This state of a hyperinflated lung volume with disturbances in lung compartment relationships, impaired blood supply and tissue atrophy in the presence of air flow obstruction bears the clinical diagnosis of *obstructive pulmonary emphysema*.

The concept of emphysema developing and progressing from air flow obstruction is not universally accepted. Rappaport and Mayer<sup>2</sup> stated that obstructive bronchitis is more often the result rather than the cause of pulmonary emphysema. It is their concept that emphysematous changes must be present in the lung in order for obstructive bronchitis to occur. These authors believe that emphysema is revealed, not produced by the signs and symptoms of obstructive bronchitis. Stead, Fry,

and Ebert<sup>7</sup> reported on the elastic properties of the lungs in patients with emphysema and stated, "It is generally accepted that the basic defect of chronic pulmonary emphysema is a loss of the normal retractive forces of the lung." This concept localizes the site of primary change within the alveolar wall. Abbott and associates<sup>8</sup> stated that focal trigger areas of bronchial obstruction may play a primary role in the pathogenesis of emphysema by reflexly stimulating pulmonary arteriolar and bronchiolar spasm via the autonomic nerves. That circulatory occlusive changes of the bronchial arteries may play a primary role in the production of lung atrophy was suggested by Cudkowiec and Armstrong.<sup>9</sup>

### PURPOSE OF STUDY

This study was designed to obtain information regarding the role of air flow obstruction as a precursor and aggravator of obstructive pulmonary emphysema. The basic approach involved relating *duration of air-flow obstruction* to the *severity of alterations in lung compartment relationships*, with particular focus on the size of the functional residual capacity (FRC) and the ratio of residual volume to total lung capacity (RV/TC). If a cause and effect relationship does exist between air flow obstruction and obstructive emphysema, such a study should provide data essential to its proof.

It was further reasoned that this information would aid in formulating decisions as to the advisability of *accepting or retaining* in military service individuals with air flow obstruction. The data would serve as aids in making a prognosis as to the individual's career and job potential in terms of future functional capacities. In such a perspective, the information has bearing on problems of disability evaluation, and is considered to represent one aspect of a broad study approach to the evaluation of disability in diseases of the chest through utilization of pulmonary function studies.

### MATERIAL AND METHODS

The 42 patients included in this study were diagnosed as having true allergic bronchial asthma. This diagnosis was based on the following criteria:

- 1 Family history
- 2 Allergic equivalents to include
  - (a) Rhinitis seasonal or perennial
  - (b) Conjunctivitis seasonal
  - (c) Sneezing
  - (d) Examination of upper respiratory passages demonstrating the characteristic "allergic mucosa"
  - (e) Eosinophils of greater than 10 per cent from either sputum, nasal secretions or blood

3 Immunologic findings to include multiple positive skin tests

4 Symptomatic relief obtained by one or more of the following measures

( ) Antihistamines

(b) Hypersensitization

(c) Environmental modifications and controls

5 Age of onset

(a) Early childhood allergies

(b) Asthma may appear in later life

The cases selected in this study satisfied a minimum of any four of the five criteria. All had multiple highly positive skin tests.

The studies were performed at a time when patients felt well and clinically were regarded as asymptomatic or free of the characteristic asthmatic attack. Patients diagnosed as having true allergic bronchial asthma were admitted to the study for the following reasons:

1 The acute clinical findings and subjective distress characteristic of the asthmatic attack serve as a relatively precise episode for dating the onset of significant air flow obstruction.

2 The air flow obstruction in bronchial asthma is a diffuse process involving the entire lung with equal intensity.

3 The acute disabling distress of the "attack" usually demands medical treatment thereby placing the patient under observation and follow up management early in the course of the disease.

The advantages of studying the sequelae of air flow obstruction in true bronchial asthma appears in sharp contrast to the difficulties and uncertainties involved in tracing and identifying etiologic relationships between *air flow obstruction* and *obstructive emphysema* in the chronic bronchitis syndrome. The clinical course in bronchitis is usually one of insidious progression without an acute dramatic attack from which one can date the probable onset of significant air flow obstruction. Air flow obstruction of a marked degree may be present when auscultation of the lungs is regarded as clear and when the patient is unaware of any increased work of breathing. As a result of the insidious nature of the disease at this stage the patient comes to the attention of the physician at a time when advanced emphysema is present. At such time one cannot distinguish chronic bronchitis from obstructive emphysema relative to cause and effect relationships. What portion of the disease complex reflects obstructive bronchitis and what portion reflects obstructive emphysema cannot be identified with any reasonable certainty. The identical clinical picture may be described by some as chronic bronchitis and by others as obstructive

emphysema Rappaport and Mayer<sup>6</sup> stated as their concept that obstructive bronchitis is usually the effect of obstructive emphysema rather than its cause

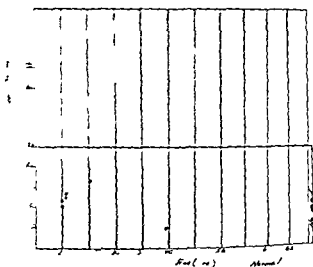
Conventional pulmonary function studies as previously described were performed on each patient<sup>10-14</sup> These included gross spirometry calculation of specific flow rates, and measurement of lung compartment volumes and relationships The functional residual capacity (FRC) is regarded as highly important in quantitating the shift of the midpulmonary position caused by hyperinflation of the lung volume It has been regarded by some as the principal difference between normal individuals and patients with pulmonary emphysema<sup>7</sup> It is reasoned that the FRC is determined by the state of balance between the passive forces of the chest wall and the retractive force of the lung The ratio of residual air to total lung volume ( $RV/TC \times 100$ ) is also regarded as an important diagnostic and quantitative expression of obstructive emphysema Therefore, the FRC and the  $PV/TC \times 100$  were selected as the principal measurements for quantitating the presence and degree of severity of the emphysematous state

Data on the per cent of predicted normal FRC and the  $RV/TC \times 100$  in 30 normal individuals, used as a control group, are presented to describe the distribution of these functions in various ages These data were included in scattergrams as a convenient means of comparing normals to the patients with bronchial asthma

## RESULTS

The scatter for FRC's (fig 1) demonstrates that 130 per cent of predicted normal is the approximate upper limit of normal in any age group The scatter in figure 2 demonstrates a variation in the ratio of residual volume to total lung volume related to age A rise in the ratio with increasing age is noted, and has been described by Baldwin Cournand and Richards<sup>15</sup> Whereas a ratio of greater than 35 per cent is generally accepted as indicating the presence of a significant degree of emphysema,<sup>1</sup> in its strictest application the ratio must be interpreted in the light of the individual's age in estimating presence and degree of emphysematous changes The data indicate that the upper limit of normal for this function, for all age groups, is 35 per cent With the exception of two cases, all normals tested, regardless of age, had a ratio of less than 35 per cent

In comparing figures 1 and 3 a significant difference is noted between the normal and asthmatic patients In the group of 42 patients, 2 with perennial and 6 seasonal asthma were within the accepted normal limit of 130 per cent of predicted normal The remaining 36 patients (85.6 per cent) were abnormal for this function Although the scatter strongly suggests that air flow obstruction is more traumatic in older patients especially



normal individuals between the two percentages of abnormality. The horizontal line at 1.0 is regarded as the upper limit of normal.

The data in figures 2 and 4 demonstrate a significant difference between normal and asthmatic patients as regards Pv/TC ratio. In the group of 42 asthmatic patients 12 (28.5 per cent) were normal whereas 30 (71.5 per cent) were abnormal. In the control group of 30 90 per cent were within normal limit. The grouping of patients with seasonal asthma in the 90 to 200 period compared with its infrequent appearance beyond 200 also suggests that with progression of time the episodic nature of the disease is replaced by perennial chronicity. The control further suggests that as the episodic type of process is replaced by perennial involvement progression into an abnormal RV/TC occurs.

emphysema Rappaport and Mayer<sup>6</sup> stated as their concept that obstructive bronchitis is usually the effect of obstructive emphysema rather than its cause

Conventional pulmonary function studies as previously described were performed on each patient<sup>10-14</sup> These included gross spirometry, calculation of specific flow rates, and measurement of lung compartment volumes and relationships The functional residual capacity (FRC) is regarded as highly important in quantitating the shift of the midpulmonary position caused by hyperinflation of the lung volume It has been regarded by some as the principal difference between normal individuals and patients with pulmonary emphysema<sup>7</sup> It is reasoned that the FRC is determined by the state of balance between the passive forces of the chest wall and the retractive force of the lung The ratio of residual air to total lung volume ( $RV/TC \times 100$ ) is also regarded as an important diagnostic and quantitative expression of obstructive emphysema Therefore, the FRC and the  $RV/TC \times 100$  were selected as the principal measurements for quantitating the presence and degree of severity of the emphysematous state

Data on the per cent of predicted normal FRC and the  $RV/TC \times 100$  in 30 normal individuals, used as a control group, are presented to describe the distribution of these functions in various ages These data were included in scattergrams as a convenient means of comparing normals to the patients with bronchial asthma

## RESULTS

The scatter for FRC's (fig 1) demonstrates that 130 per cent of predicted normal is the approximate upper limit of normal in any age group The scatter in figure 2 demonstrates a variation in the ratio of residual volume to total lung volume related to age A rise in the ratio with increasing age is noted, and has been described by Baldwin, Cournand and Richards<sup>15</sup> Whereas a ratio of greater than 35 per cent is generally accepted as indicating the presence of a significant degree of emphysema,<sup>1</sup> in its strictest application the ratio must be interpreted in the light of the individual's age in estimating presence and degree of emphysematous changes The data indicate that the upper limit of normal for this function, for all age groups, is 35 per cent With the exception of two cases all normals tested, regardless of age had a ratio of less than 35 per cent

In comparing figures 1 and 3 a significant difference is noted between the normal and asthmatic patients In the group of 42 patients, 2 with perennial and 6 seasonal asthma were within the accepted normal limit of 130 per cent of predicted normal The remaining 36 patients (85.6 per cent) were abnormal for this function Although the scatter strongly suggests that air flow obstruction is more traumatic in older patients, especially



those above 45 years, 3 patients below 40 years of age had an FRC that was greater than 260 per cent of predicted normal. This is considered as a severe degree of expansion for this lung compartment. The scatter also suggests that perennial asthma is more traumatic on this lung compartment than the seasonal type. Of the 14 patients with seasonal asthma 7 were within normal range and 7 were abnormal. In the 28 patients with perennial asthma 3 were normal and 25 were abnormal.

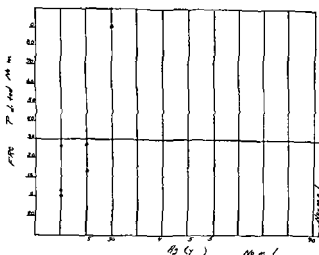


Figure 1. Relationship between age and relative functional residual capacity. The horizontal line represents 100 per cent of predicted normal. The vertical line represents 38 ml per cent of predicted normal.

The data in figures 2 and 4 demonstrate a significant difference between normal and asthmatic patients as regards RV/TC ratio. In the group of 42 asthmatic patients 12 (28.5 per cent) were normal whereas 30 (71.5 per cent) were abnormal. In the control group of 30 95 per cent were within normal limits. The close grouping of patients with seasonal asthma in the 20 to 25 year period compared with its infrequent appearance beyond this age suggests that with progression of time the episodic nature of the disease is replaced by perennial chronicity. The scatter further suggests that as the episodic type of process is replaced by perennial involvement progression into an abnormal RV/TC occurs.

Figure 5 demonstrates that the FRC in patients with seasonal asthma is less affected by duration of symptoms than in patients with perennial asthma. In 14 patients with seasonal asthma, 7 were within normal limits, whereas only 3 (10.7 per cent) of 28 patients with perennial asthma were normal. Four patients with seasonal asthma had symptoms in excess of 15 years. The 3 patients with perennial asthma normal for this function had

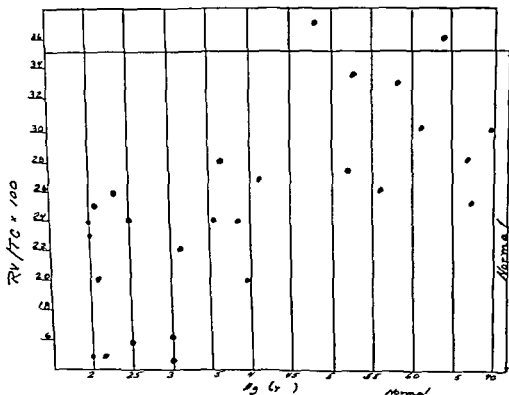


Figure 2 Relationship between the ratio of residual volume to total lung volume ( $RV/TC \times 100$ ) and age in normal individuals. The horizontal line at 35 per cent is taken as the upper limit of normal for all age groups.

symptoms for less than 11 years. In the 17 patients with symptoms of less than 11 years duration, only 3 had an FRC greater than 170 per cent of predicted normal. The remaining 14 (78.8 per cent) had a normal or only minimally elevated FRC. Twenty-four patients had symptoms in excess of 11 years. Nine of these 24 (37.5 per cent) had a normal or only minimally elevated FRC, whereas 15 (72.5 per cent) had an elevation of the FRC greater than 170 per cent of predicted normal. Eighty-nine per cent of patients with perennial asthma, symptomatic in excess of 11 years, developed an elevation of the FRC greater than 170 per cent of predicted normal.

Figure 6 demonstrates that a significant rise in the FFC occurred with prolongation of symptom. The figure illustrates

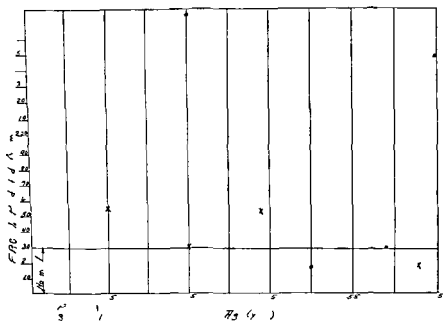


Fig 3 Rlt b p b tw en th per t pr d t d m l f n t al  
dual c pac ty d ag p t t w th e al d p l a thma  
Th bo zo t l l at 130 per t g a d d a th p p e r l m t of o r m l

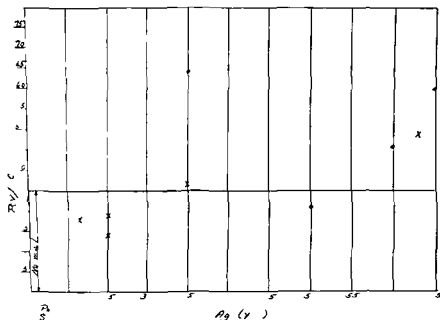


Figure 4 Rlt b p b tw th t t f r d l vol m t t t l l g  
l m (RV/TC 100) a d ag pat t w th as l and per l  
a thma Th bo t l l at 35 per t t g d d a th p p l m t  
f n o m l

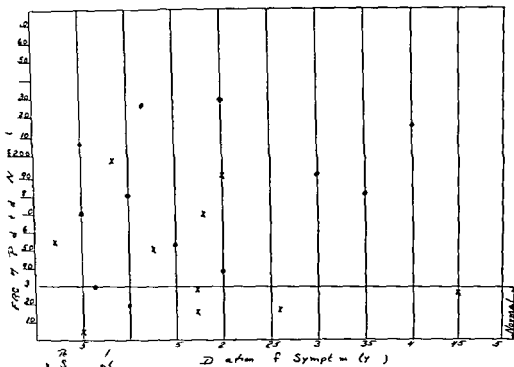


Figure 5. Relationship between the percent predicted normal functional residual capacity and duration of symptoms in patients with seasonal and chronic asthma. The horizontal line at 130 per cent is regarded as the upper limit of normal.

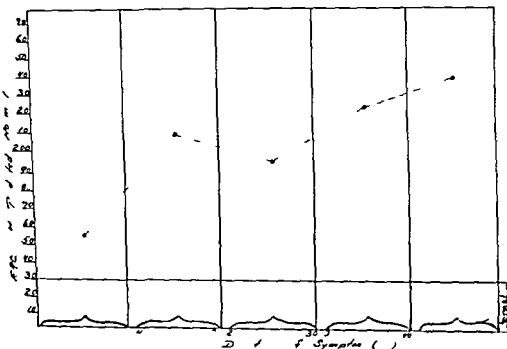


Figure 6. Relationship of the average percent predicted normal functional residual capacity and the duration of symptoms in patients with seasonal asthma. The percent predicted normal functional residual capacity is the average for the patient exhibiting symptoms within the first year of illness indicated.

that duration of symptoms beyond 10 years resulted in the development of a more severe degree of abnormality in the size of this lung compartment. It indicates that duration of symptoms (air flow obstruction) carries the risk of producing a degree of hyperinflation that makes it extremely unlikely that any significant degree of reversal in the disturbance can be obtained.

The high degree of scatter demonstrated in figure 7 for the RV/TC is so great that one may reasonably conclude that this function unlike the FRC is not dependent upon duration of symptoms for degree of abnormality. This is consistent with the fact that the RV/TC unlike the FRC is dependent upon

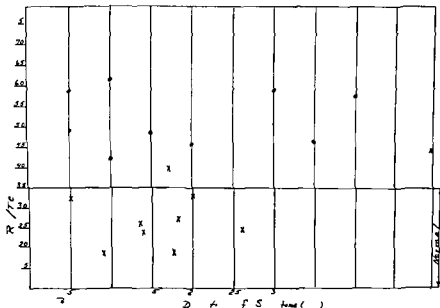


Figure 7 Relation between the ratio of RV/TC (RV/TC  $\times$  100) and duration of symptoms in years for a patient with asthmatic and peripheral emphysema. The horizontal line at 35 represents the normal limit.

the expiratory capacity. The expiratory capacity may be highly variable depending on the nature of the patient's effort, and the degree of air flow obstruction. Because the FRC is independent of the patient's expiratory effort, it is free of fortuitous influences.

### CONCLUSIONS

A marked increase in the size of the FRC and RV/TC was demonstrated in asthmatic patients during the so-called asymptomatic period. These changes were considered to indicate that air flow obstruction, air trapping, and hyperinflation of the lung volume were present at a time when patients were considered

to be well controlled, and auscultation was entirely to relatively free of wheezes and rhonchi. A relationship was noted to exist between *duration of air flow obstruction* and *size of the FRC*. Prolongation of air flow obstruction resulted in a progressive alteration of the lung volume (hyperinflation) characteristic of obstructive emphysema. This relationship was not found to exist between RV/TC and duration of symptoms. An explanation for this was presented.

Seasonal asthma did not result in the degree of abnormality in lung volume relationships that was demonstrated in the perennial variety. The data suggested that seasonal asthma became perennial after 10 to 15 years.

The data strongly suggested that the "golden era" for control of air flow impairment and prevention of irreversible large lung volume disease was within the first 10 to 15 years following onset of symptoms. Symptoms in excess of 10 years resulted in an elevation of the FRC that was greater than 190 per cent of predicted normal in the vast majority of cases studied (table 1).

TABLE 1 Mean average for functional residual capacity as per cent of predicted normal according to duration of symptoms

Duration of symptoms years	Mean average functional residual capacity as per cent of predicted normal
0 to 10	156
11 to 20	214
21 to 30	196
31 to 40	228
41 to 50	240

The evidence indicated that even during the so called asymptomatic period, significant air flow obstruction and resultant air trapping and hyperinflation of the lung volume exist in asthmatic patients. This implies the need for continuous medical management. The absence of wheezes and rhonchi in these patients must not be accepted as evidence that air flow obstruction is not present.

The effect of bronchodilator drugs on the lung compartments in allergic asthma is an important consideration. A basic aim in using these agents is to aid in determining whether bronchospasm with acute hyperinflation or obstructive emphysema is complicating the allergic state. The interpretation of physiologic studies before and after bronchodilator drugs is difficult, controversial, and involves a multiplicity of considerations and variables such as (1) What degree of change in function after therapy is significant? (2) Which function studies are most sensitive to change following this therapy? (3) Which of several studies shall be regarded as most sensitive in making a differen

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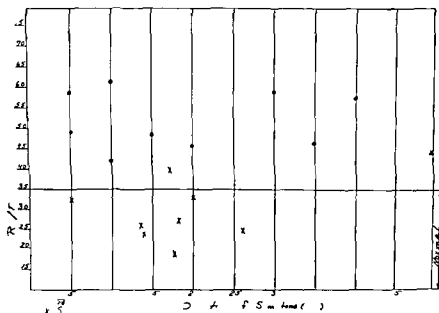


Fig. 7. Relation between the ratio of RV/TC (RV/TC  $\times$  100) and duration of symptoms in patients with asthmatic and perennial asthma. The horizontal line at 35 percent is regarded as the upper limit of normal.

the expiratory capacity. The expiratory capacity may be highly variable depending on the nature of the patient's effort and the degree of air flow obstruction. Because the FRC is independent of the patient's expiratory effort, it is free of fortuitous influences.

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## BEFORE AND AFTER ATHEROSCLEROSIS

Many patients operated upon for aneurysms and occlusive disease are in the later decades of life and have a relatively short life expectancy. Thus the time from operation to death is an opportunity to investigate certain aspects of lipid metabolism as it relates to atherosclerosis. At op- eration the diagnosis of atherosclerosis could be made with certainty and the type and extent of the atheromatous lesions recorded. Subsequently at necropsy whether months or years later the arterial system could be re examined and the findings compared with those obtained previously. Thus a series of before and after observations would be avail- able against which factors such as the natural history of the disease, metabolic alterations, and effectiveness of drug therapy could be evaluated. To a surgeon at least this sort of investigation is more appealing than one in which the diagnosis is based solely upon clinical man- ifestations, the electrocardiogram and blood lipids, and in which the same indirect criteria are employed in evaluating results.

—OSCAR CREECH Jr M D  
in *American Heart Journal*  
P 642 Nov 1957



# DISSEMINATED COCCIDIOIDOMYCOSIS TREATED WITH AMPHOTERICIN B

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EDWARD S MONGAN M D

**S**INCE amphotericin B became available to us more than a year ago we have had under observation at this hospital nine patients with disseminated coccidioidomycosis. Five were eliminated from the study: two because they had already undergone a clinical and serologic remission; one because he was improving rapidly when the diagnosis was established; one because he had only serologic evidence of dissemination; and one because he had far advanced disease and died the day of admission. This report describes the results obtained in the treatment of the remaining four patients with amphotericin B.

## AMPHOTERICIN B

Amphotericin B is an antibiotic derived from a species of *Streptomyces* found in a soil sample from the Orinoco River basin in Venezuela. In vitro it has been shown to have antifungal properties for a wide variety of organisms, including *Coccidioides immitis*. In vivo it has had an ameliorating effect on mice experimentally infected with *C. immitis*. In neither animals nor humans was there significant toxicity when the drug was given orally, possibly because of its poor absorption from the gastrointestinal tract.

The LD for intravenous administration in mice was 8 mg per kg. All of the mice that died did so within nine minutes of the infusion with symptoms of ataxia, spasms, and terminal collapse. Littman, Horowitz, and Swadey described one patient who received 28 mg intravenously in 40 minutes. He had convulsions and cardiac standstill but recovered. Anorexia, nausea, vomiting, chills, and fever have occurred commonly during and shortly after intravenous administration. Such reactions may have been minimized by use of salicylates and antihistamines. On prolonged intravenous administration there was a tendency for the blood urea nitrogen to increase, but this has subsided with temporary interruption of therapy.

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The poor absorption of amphotericin B given by mouth has led to preference for the intravenous route of administration. The toxicity has necessitated slow infusion and limited dosage. It is currently recommended that the water-soluble salt be dissolved in sterile 5 per cent dextrose in water to a concentration of 1 mg per 10 ml. The solution should be infused slowly intravenously over a period of six hours or more to a maximum dose of 1 mg per kg daily.<sup>1</sup> Littman, Horowitz, and Swadey<sup>2</sup> suggested a maximum dose of 1.6 mg per kg, and believed that infusion on alternate days reduced the chances of nitrogen retention.

Lehan and associates<sup>3</sup> stated that in several instances when administered intravenously, the amphotericin B infiltrated into surrounding subcutaneous tissue. Mild discomfort and redness at the site resulted, but the complication was not serious. Littman, Horowitz, and Swadey repeatedly injected amphotericin B into a knee severely involved with coccidioidomycosis. The drug was well tolerated and appeared to benefit the knee.

#### TREATMENT OF COCCIDIOIDOMYCOSIS

The acute pulmonary form of coccidioidomycosis is generally a benign, self-limited disease. It offers no serious therapeutic problems, although it produces prolonged morbidity at times. Occasionally, a residual granuloma or cavity in the lung requires surgical removal, but the majority of these are asymptomatic and yield to expectant treatment.

The disseminated disease is relatively rare and far more serious, with a mortality of about 50 per cent. In the past 20 months we have treated 14 patients with disseminated coccidioidomycosis with five deaths to date. In one, the course was fulminating and death occurred two weeks after the onset.<sup>4</sup> Others have recovered spontaneously.<sup>5</sup> Still others have followed a chronic and slowly progressive downhill course.

Evaluation of the therapy of disseminated coccidioidomycosis has been difficult because of the irregular course of the disease. The literature has been contradictory on the subject. However, there has been no good evidence that any therapeutic agent in the past has favorably influenced the course of disseminated coccidioidomycosis.<sup>2-6</sup> To the long list of ineffective agents we have added chloroquine diphosphate. We had two patients who recovered following the use of chloroquine. Our initial enthusiasm was properly curbed when this drug clearly accomplished nothing for the next seven patients with the disseminated disease.

The collection of clinical data on the therapeutic trial of amphotericin B for disseminated coccidioidomycosis has been slow. There has been little upon which to draw conclusions. Klapper, Smith, and Conant<sup>7</sup> and Yiser<sup>8</sup> each reported one case in which apparent benefit resulted from the oral administration

of amphotericin B Littman Horowitz and Swadev reported two cases in which improvement coincided with intravenous amphotericin B Preliminary reports to the Squibb Institute for Medical Research included four additional cases two on oral therapy and two on intravenous therapy The results were encouraging

### CASE REPORTS

C 1 A 34 year-old Negro was admitted to this hospital on 10 December 1956 complaining of chest pain About one month earlier he had noted the onset of fever malaise easy fatigability shortness of breath right-sided pleuritic type pain cough and occasional hemoptysis He had been stationed in El Paso for six months in 1950 and again for nine months prior to admission

On examination he appeared well developed well nourished and in no distress His height was 70 inches weight 215 lb temperature 98.0 F pulse 80 blood pressure 120/82 mm Hg There was slight dullness and decreased breath sounds over the right lung base posteriorly Roentgenograms of the chest showed scattered nodular densities the left lung an infiltrate in the right lung base and right hilar lymphadenopathy

The white blood cell count was 11,600 per  $\mu$ l with 26 per cent eosinophils The hemoglobin 13.5 grams per 100 ml *C. immittis* was cultured from the sputum Reaction to the coccidioidin skin test was positive Complement fixation for coccidioid mycosis was positive in a titer of 1:64

One month after admission a 3 by 6-cm mass of lymph node was noted in the right supraclavicular area A specimen for biopsy showed a granulomatous reaction with numerous giant cells containing thick-walled spherules and endospores Culture of the material was positive for *C. immittis* An abscess appeared at the biopsy site and culture of the pus was positive for *C. immittis* A draining sinus persisted in this area for three months after which it healed spontaneously

In March 1957 a coccidioidal abscess developed in the middle phalanx of the fourth toe on the patient's left foot This was incised and drained The resulting sinus healed about a month later

During the first two months in the hospital the patient's general condition remained good but he lost 35 lb in weight By early June his infection appeared to be under control A roentgenogram of his chest was clear and there was no evidence of active lesions On 6 June therapy with amphotericin B by mouth was initiated the patient receiving approximately 5 grams daily for 38 days The drug was well tolerated

His complement fixation for coccidioidomycosis was 1:16 on 27 June and 1:8 on 5 July He was discharged to duty on 7 August

On follow up examination on 13 February 1958 he appeared well. Blood cell count and roentgenographic findings of the chest were normal. His complement fixation was 1/4.

**Comment** This patient was on the road to recovery when treatment with amphotericin B was started. There was no reason to believe that the drug altered the course of his disease.

**Case 2** A 40 year old Negro was admitted to this hospital on 28 January 1957 complaining of malaise and cough. For the preceding two weeks he had had low grade fever, night sweats, headache, malaise and cough productive of small amounts of yellow sputum. He had been stationed in El Paso for two and one half years.

Examination revealed a somewhat obese man who was not in acute distress. His height was 69 inches, weight 200 lb, temperature 99.1°F, pulse 88 and his blood pressure was 125/75 mm Hg. There were dullness and fine rales over the right lung base posteriorly. There was a single 3 mm granuloma in the skin of the dorsum of the right wrist. A roentgenogram of the chest showed a pneumonitis in the right lung base and right hilar lymphadenopathy.

The white blood cell count was 7,500 per  $\mu$ l with 14 per cent eosinophils. The hemoglobin was 13.5 grams per 100 ml. Coccidioidin skin tests were negative throughout the course of his disease. *C. immitis* was cultured from his sputum. Complement fixation for coccidioidomycosis was negative.

About one month after admission a hard mass was noted in the right supraclavicular area. It gradually increased in size and became fluctuant. On 5 April it was incised. *C. immitis* was recovered from the pus. Three months after admission the patient had lost about 30 lb in weight, his complement fixation for coccidioidomycosis had become positive in a titer of 1/256 and numerous new granulomata had appeared in the skin. *C. immitis* was identified microscopically and by culture in several of the skin lesions. The granulomas tended to break down leaving indolent ulcers 1 to 3 cm in diameter draining bloody purulent material (fig. 1).

Six months after admission the patient's condition stabilized. He regained his normal weight and appeared healthy with the exception of the ulcerations of his skin. His complement fixation had dropped to 1/64. A roentgenogram of the chest showed no change since admission.

In September, nine months after admission, amphotericin B was started, 45 mg intravenously every other day. The patient regularly had chills, fever and vomiting during and up to 12 hours after administration of the drug. In November treatment was discontinued for two weeks because of elevation of his blood urea nitrogen. Between 22 September and 18 December he received a total of 1,125 mg of amphotericin B.

While on therapy all of his skin lesions healed, roentgenographic findings of his chest became normal.

including the presence of the organism. The complement fixation for coccidioidomycosis was positive in a titer of 1:32. The lesion in the lumbar spine was presumed to be caused by coccidioidomycosis.

On 25 February amphotericin B intravenously was again started. The dose was rapidly increased to 50 mg every other day. The patient had chills and fever with each administration. In late March the drug was stopped for two weeks because of nitrogen retention. By 30 May he had received an additional 1890 mg of the drug and a total of 4440 mg intravenously. There has been no significant change in his condition on the last course of treatment and he continued to appear well except for the limitation in motion of his neck. His complement fixation had dropped to 1:16 in May.

**Comment.** This patient was severely ill and bedridden when amphotericin B was started. Improvement was noted coincidentally with the use of the drug. The evidence was suggestive that the drug was beneficial. Particularly notable was the rapid subsidence of the indolent abscess of his rib when injected locally with amphotericin. The appearance of new lesions of the skin and bone in February 1958 indicated continued dissemination in spite of the falling titer on the complement fixation test.

**CASE 4.** A 22-year-old Negro was admitted to the hospital on 15 January 1958. In early December 1957 he had noted the onset of chills, fever, malaise, myalgia, back pain, nonproductive cough, anorexia, and a weight loss of 15 lb. He had been admitted to Brooks Air Force Base dispensary, El Paso, Texas, on 4 January 1958. There he was found to have fever, lymphadenopathy in the inguinal and anterior cervical regions, and a small papule over the right eye. His white blood cell count was 24,000 per  $\mu$ l with 30 per cent eosinophils. He had been stationed in the El Paso area for 18 months.

Examination showed a thin, asthenic and chronically ill man who had lost a total of 25 lb in weight. His height was 68 inches, weight 135 lb, pulse 96, respirations 30 per minute, temperature 102.1 F, and his blood pressure was 140/87 mm Hg. There were numerous lymphadenomegalies 2 to 3 cm in diameter in the anterior cervical, femoral, and inguinal areas. The liver was palpated 3 cm below the costal margin, and the spleen at the costal margin. There were scattered granulomatous skin lesions measuring 6 to 8 mm in diameter. There was one larger skin lesion over the right eyebrow measuring 1.5 cm in diameter and 0.6 cm elevated (fig. 2). A roentgenogram of the chest showed an infiltration in the right cardiophrenic angle and bilateral hilar lymphadenopathy.

The white blood cell count was 20,550 per  $\mu$ l with 10 per cent eosinophils. His hemoglobin was 11.8 grams per 100 ml. The coccidioidin skin test remained negative in monthly testing. *Coccidioides immitis* was cultured from the lesion above the right eye from pus aspirated from an anterior cervical lymphadenomegaly and repeatedly from the sputum. Biopsy of the skin lesion above the right eye revealed a

granuloma containing numerous thick walled organisms with endospores. Complement fixation test for coccidioidomycosis was 1/16.



Figure 2 (case 4) *Coccidioidal granulomata on the face*

Treatment with amphotericin B intravenously was initiated on 24 January. By 30 May the patient had received a total of 2,970 mg in four months. The dosage eventually was stabilized at 50 mg every other day. The patient routinely had severe febrile reactions on each administration. On two occasions a rise in his blood urea nitrogen necessitated temporary cessation of treatment.

On different occasions pus was aspirated through a 16 gage needle from six enlarged fluctuant nodes in the neck, groin and femoral areas and 25 mg of amphotericin B dissolved in 25 ml of water was injected. Four were injected twice. There was no apparent local irritation to this procedure. Although he was receiving intravenous medication at the time *C. immitis* was cultured from the pus from most of the nodes. All of the locally treated lesions decreased in size and became nonfluctuant over a period of 3 to 6 weeks after injection (figs 3 and 4) but only one had completely disappeared.

His condition on admission was poor. He had a septic fever with a temperature of 103 to 104°F daily and little appetite. One week after admission he began to complain of severe pain in the right upper abdominal quadrant. On examination he had tenderness and rigidity of the abdominal wall in this area. There also was a partial paralytic ileus with considerable abdominal distension. The fever subsided to generalized abdominal tenderness and moderate leukocytosis.

abdominal paracentesis was not performed but the findings and course were thought compatible with coccidioidal peritonitis. The patient's condition appeared to be terminal at this time and he was carried on the seriously ill list. He had anemia severe enough to require four blood transfusions during his second month in the hospital.



Figure 3 (4) Coccidioidal abscesses subcutaneous lymph nodes shortly after they were first treated with amphotericin B.

In March gradual and persistent improvement began. His ascites diminished, his appetite improved, the lymphadenopathy decreased, the hemoglobin stabilized at 10 grams per 100 ml and the skin lesions decreased in size. His fever continued but the daily peaks were lower, 100 to 101 F. His strength returned and he was able to ambulate partially. No new lesions of the skin, lymph nodes or bone appeared after amphotericin B was started on 24 January. The patient was far from well but by May was much improved. In spite of the clinical improvement his complement fixation rose from 1:16 on admission to 1:128 five months later.

**Comment:** This patient was moribund when treatment with amphotericin B was started. We were fearful that he would be unable to tolerate the toxic reactions to the drug. At the same time the prognosis in a Negro patient with disseminated coccidioidomycosis of this severity is so unfavorable that it did not appear

reasonable to withhold treatment. His improvement was not dramatic but it was impressive. There was no complement fixation increase as he improved clinically.



Figure 4 (case 4) Same area shown in figure 3, in week 4 of second injection of amphotericin B into a vein.



Our use of amphotericin B by mouth was limited to a short course of 38 days given to the first patient. Although the patient recovered we were unable to draw any conclusions on this mode of administration.

The three patients who received amphotericin B intravenously reacted predictably with anorexia, nausea, chills, and fever on every administration. The reactions tended to decrease slightly in severity with continued medication but remained severe after months of treatment. Salicylates and antihistamines were ineffective in our hands in altering the reactions. All three patients had an elevated blood urea nitrogen one or more times during treatment. This subsided on each occasion upon interrupting therapy for one or two weeks. Because of the unfavorable reactions we were unable to exceed a dose of 50 mg (0.7 to 0.9 mg per kg) given over a six hour period every other day. This particular dosage may have been prompted to some extent by the packaging of the amphotericin B in 50 mg vials. Littman, Horowitz, and Swadey<sup>7</sup> independently arrived at the same conclusion as to frequency of medication but were successful in giving larger doses. Our patients suggested that the infusions be started immediately after supper so as not to interfere with food intake. This was a useful consideration in treating a disease in which weight loss, malnutrition, and poor body resistance were important factors.

The results of treatment in a disease as unpredictable as disseminated coccidioidomycosis must be accepted with caution. Our three patients improved while on intravenous amphotericin B therapy. It appeared likely that the favorable course of the disease was in part brought about by the drug. The response if any was slow. We were still able to culture *C. immitis* from a variety of areas in these patients after they had been treated intravenously with amphotericin B for months. We were unable to avoid speculating as to what might have been accomplished had we been able safely to give 10 or 100 times as much drug intravenously.

We injected amphotericin B into 7 coccidioidal abscesses: 1 in bone and 6 in lymph nodes. Two were injected once, 4 twice, and 1 three times, with about a week between injections. Positive cultures were obtained from nearly all of the abscesses although the patients were receiving amphotericin B intravenously at the time. The dose was 20 to 25 mg dissolved in 9.5 ml of water. There were no untoward local or systemic reactions to the injections. All of the abscesses had been present for several months and were either stationary or increasing in size when local treatment was started. The response was uniformly favorable. Two lesions healed completely in four to six weeks. The other five lesions decreased in size and became nonfluctuant in three to six weeks, but a residual firm mass remained. There seemed to be little doubt that the injection of amphotericin B

directly into coccidioidal lesions was effective and useful. We believed that the relatively high concentration obtained in the abscess cavities explained the excellent response.

Smith<sup>9</sup> believed that the abdominal pain, partial ileus, and ascites in the fourth patient were manifestations of coccidioidal peritonitis. Retrospectively, diagnostic paracentesis and intra peritoneal injection of amphotericin B would have been desirable and possibly beneficial. At the time this report was written, the patient had improved to the extent that this measure was no longer under consideration.

The results obtained with amphotericin B intravenously indicated that it possibly was useful in treating disseminated coccidioidomycosis. The results obtained with direct injection of coccidioidal abscesses were more impressive. Amphotericin B in all probability represents the first real advance in the treatment of disseminated coccidioidomycosis, but further clinical testing will be essential. A similar agent with equal effectiveness but less toxicity could prove to be the answer to the therapy of coccidioidomycosis.

#### SUMMARY

Four patients with disseminated coccidioidomycosis were treated with amphotericin B, one orally and three intravenously. The usefulness of the oral drug was not determined. The three patients on the intravenous preparation were treated for periods of 3 to 12 months. All improved while on therapy. Amphotericin B administered intravenously regularly caused chills, fever, anorexia and nausea during and shortly after each infusion. Salicylate and antihistamines did not alter these reactions. Azotemia occurred one or more times in each patient on intravenous therapy, but subsided upon interrupting treatment for one or two weeks. The unfavorable reactions were minimized by limiting the dose to 20 mg given every other day immediately after supper. The water-soluble salt was dissolved in 5 per cent dextrose water to a concentration of 1 mg per 10 ml and infused slowly. Six hours or more were taken for each infusion.

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## MODERN SCIENCE AND CIVILIZATION

As an instrument science can achieve either good or ill. That will depend upon the minds and spirits of those who use the instrument. Our natural and acquired capacity for extravagance skillfully played upon by the sensationalists of the fleeting day can too easily lead us to believe that the need for more scientists is such that all other higher studies should be subordinate; that the study of physical nature is the only thing that greatly matters; that if knowledge comes wisdom will not linger. Believing as I do that science and wisdom have no necessary connection and that scientific study and achievement are not ends but means I am driven to the conclusion that what the scientists do or will do will put into our hands discoveries which can be the means of destruction or of a new and complicated form of technological slavery but which wisely used can be the means of human salvation. The answer will depend upon our character, our broad intelligence and our wise and understanding judgment.

—R G MENZIES

Th M d l f m l f A t l  
p 516 Ap 19 1958



## Clinicopathologic Conference

Walter Reed Army Hospital Washington, D C •

### WEAKNESS OF ONE YEAR'S DURATION

**Summary of Clinical History** A 59 year old retired officer was admitted to this hospital for the second time on 22 July 1957. He apparently was well until January 1955 when an annual physical examination revealed albuminuria. He was asymptomatic and refused hospitalization for diagnostic study. In June 1955, he noted ankle swelling and decrease in exercise tolerance. The following September he was retired from the Army. During the following year, he noticed increased fatigability and numbness and paresthesia in his left knee. In October 1956, he was seen in the out patient clinic where he was found to have hypertension. Urinalysis revealed a specific gravity of 1.020 and albuminuria ranging from 1 plus to 4 plus. The phenolsulfonphthalein excretion was 9 per cent in 15 minutes and 24 per cent in two hours. There was bilateral pitting ankle edema. Because of this edema, the patient was given digitalis and a course of phenobarbital and Serpasil (brand of reserpine), 0.25 mg three times a day. Laboratory studies performed at this time revealed a blood urea nitrogen of 17.7 mg per 100 ml and a total serum protein of 5.4 grams (albumin, 2.2 grams, globulin, 3.1 grams) per 100 mL. An intravenous pyelogram was interpreted as normal.

This is one of many cases which does not fit into the old classification of primary and secondary amyloidosis a division which in the light of modern concepts appears obsolete

### Pathologic diagnoses

- 1 Primary amyloidosis involving kidneys spleen adrenals liver pancreas and bone marrow
- 2 Arteriosclerosis and hypertensive cardiovascular disease

### COMMENTS

**D r S p i** The concept of amyloidosis as a systemic disease was developed by Rudolph Virchow. He established the distribution of organ lesions and the histopathology and considered the disease to be a derangement of cellular metabolism. The various manifestations and organ involvement in amyloidosis had been noted for centuries by various observers but it remained for Virchow's keen insight and accurate power of observation to bring them under a common denominator. He had studied some of the rather characteristic color reactions which are elicited by Lugol's solution and sulfuric acid on amyloid.

Under the mistaken belief that he was dealing with a starch or cellulose-like compound he gave the disease its name amyloidosis under which it is still known today. Virchow announced his discovery to the general medical public in one of a series of 20 lectures which he delivered in the spring of 1858 at the University of Berlin. The lectures created a sensation in their day and were published in the same year in book form. This book *Cellula Pathology* has remained a classic. It went through many editions and was translated into every civilized language. It is one of the most influential books in modern medicine.

It is a peculiar fact that very little has been added to our knowledge of amyloidosis in the past 100 years. We know now that it is a proteaceous substance the exact composition of which has yet to be determined. We are still in the dark about the mechanism of its deposition and its eventual removal. In its so-called secondary form it is associated with and is a complication of long standing suppurative infection such as chronic osteomyelitis and tuberculosis. It may appear within the matter of a few months but more frequently it occurs after a period of years following the establishment of a chronic infection or debilitating condition. Its progress is variable. Since the advent of modern therapy which has practically eliminated such prolonged suppurative diseases secondary amyloidosis has become a rarity. A mal-experimentation has thrown little light on its pathogenesis. We know that marked peculiar differences exist in the ease in which amyloidosis can be produced in susceptible animals. Amyloidosis follows flooding the body with foreign protein. This has given rise to the hypothesis that an *in vivo* antigen body antigen reaction is involved with precipitation.

of amyloid at the reaction sites. Different chemical composition of antigen and antibody could then account for the observed chemical differences in the composition of amyloid. Preferred sites of amyloid deposition are cells of the reticuloendothelial system, a fact which may be associated with the hyperglobulinemia not infrequently observed in amyloidosis.

When we attempt to correlate the autopsy findings with the clinical evolution of the disease in our patient we note that the long standing, mild to moderate hypertension is reflected in the moderately severe concentric hypertrophy of the heart which characteristically was only slightly enlarged on roentgenographic examination. In addition the patient had a severe degree of coronary sclerosis with myocardial scarring. His arteriosclerotic hypertensive heart disease undoubtedly was aggravated by the progressive renal failure incident to the amyloidosis to which he eventually succumbed. As previously stated, however the heart was free of amyloid deposits. The albuminuria first noted in January 1955 was most likely the initial manifestation of renal involvement by amyloid. Proteinuria is an almost invariable accompaniment of renal amyloidosis although for reasons yet unknown there is no correlation between the amount of amyloid deposited in the kidney and the degree of albuminuria. Unfortunately in our case the urinary proteins were not studied electrophoretically. It is said that of all conditions leading to proteinuria renal amyloidosis is associated with the highest admixture of globulin. While in lipid nephrosis for instance the albumin globulin ratio of urinary protein is about 10 to 1 in renal amyloidosis it is often less than 5 to 1 and may even approach a ratio of 2 to 1. The pitting ankle edema which was first noted in June 1955 was probably due to a combination of low plasma albumin and mild heart failure. The Addison count performed in December 1956 reflects the predominantly glomerular involvement in renal amyloidosis. As more and more glomerular tufts became obstructed by amyloid deposits the specific gravity of the urine dropped from 1.020 to 1.010. The progressive atrophy of nephrons accounts for the unremitting renal failure. At autopsy every glomerulus was severely affected and not a single normal nephron had remained. The amyloid deposits in the remainder of the organs apparently had little functional significance. Even the marked involvement of the adrenals had not led to any signs or symptoms of Addison's disease.

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# CASE REPORTS

## Collision Tumor

ROBERT C THOMAS *Leutenant MC USN*  
ALBERT CANNON *Leutenant Commander MC USN*

**I**N a collision tumor a sarcoma invades a carcinoma or vice versa. There are numerous reports in the literature concerning various types of carcinosarcomas<sup>1</sup> but few have been generally accepted as true carcinosarcomas. A case of collision tumor in which both the carcinomatous and the sarcomatous elements have metastasized and which is thought to be a true case of dual malignancies developing in juxtaposition is presented.

### CASE REPORT

A 69 year old retired chief petty officer was admitted to the U S Naval Hospital Annapolis Md complaining of difficulty in swallowing solid food. He had been well until four weeks prior to admission when he noticed the onset of a sore throat and pain in the left side of his neck. Dysphagia for solid food developed thereafter. A large fungating polypoid lesion was found on the posterior aspect of his tongue to the left of the midline. A biopsy specimen was reported as demonstrating anaplastic squamous cell carcinoma and the patient was transferred to the U S Naval Hospital Bethesda Md for treatment.

Physical examination on admission to this hospital disclosed a mushroomlike lesion measuring 2 by 3 by 5 cm attached to the posterior part of the tongue to the left of midline by a short relatively narrow pedicle 1.5 cm in diameter and partially occluding the oropharynx. The mass was friable bleeding easily with trauma. Induration extended laterally into the floor of the mouth medially to the midline of the tongue and inferiorly into the neck to a point just superior to the hyoid bone. No discrete nodes were palpated. Advanced peripheral arterial changes in both legs more marked on the right were evident. Pulses were absent below the femorals bilaterally.

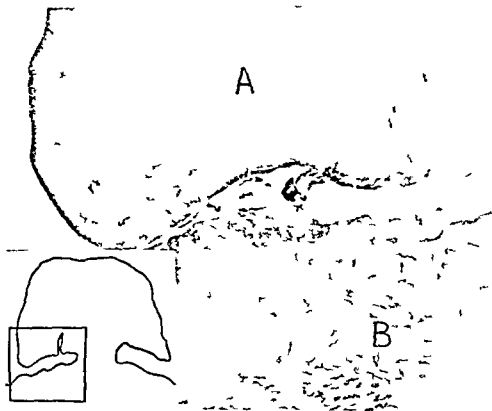
Routine laboratory studies including blood cell counts urinalysis and roentgenograms of the chest mandible and skull were within normal limits.

The tumor board recommended that the lesion be removed surgically. This was accomplished on 27 November 1957 by a left hemiglossectomy and with radical neck dissection. A tracheotomy was performed and a Levin tube placed for feeding.

*From US Naval Hospital Bethesda Md.*

Postoperatively the patient showed moderate confusion which was thought to be a result of arteriosclerosis. This quickly cleared. The operative sites healed well. The patient's progress was rapid and he was soon taking full oral feedings. Unfortunately ten days postoperatively the patient developed further ischemic changes in his right leg which progressed to frank dry gangrene in spite of treatment by peridural block and anticoagulants. An above knee amputation was necessary from which recovery was uneventful.

**Pathologic Findings** After review of multiple sections of the surgical specimen (figs 1-6) the diagnosis of a true collision tumor was made. The epithelial part of the tumor (figs 3 and 6) was unquestionably a squamous cell carcinoma showing both deep invasion of the tongue and metastases to nodes.



*Figure 1. A cross section through the tumor and the base of the tongue. The insert shows a diagram of the entire lesion with the area in this section outlined. "A" is part of the large polypoid growth while "B" shows nests of malignant squamous cells in various degrees of differentiation at the base of the tongue ( $\times 30$ ).*

The interpretation of the sarcomatous elements (figs 2 and 4) presented some difficulty. There was little question of malignancy which was evidenced both by deep invasion of the tongue musculature (fig 4) and by metastases to lymph nodes (fig 5). In both the primary site and the metastases the appearance was the same: a markedly pleomorphic and fusiform arrangement that had the general appearance of a rhabdomyosarcoma. However, cross striations were visible in





Fig 2. Photomicrograph of a section of the maxillary mandible (Fig 1) showing the arrangement of the cells ( $\times 100$ )



Figure 3. Photomicrograph of a section of the tongue (Fig 1) showing the arrangement of the cells ( $\times 100$ )

only a rare cell making this diagnosis questionable. Special stains such as Masson's trichrome and reticulum stains indicated that the

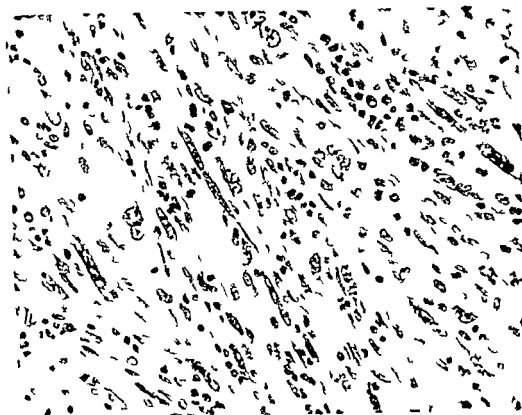


Figure 4 Sarcomatous tissue deep within the tongue musculature. Remnants of muscle fibers of the tongue are visible in the center of the figure ( $\times 200$ )

tumor was a sarcoma of muscle origin rather than a fibrosarcoma. The diagnosis therefore was either a leiomyosarcoma or an undifferentiated rhabdomyosarcoma.

#### DISCUSSION

Multiple tumors of the carcinosarcoma type have been classified by Saphir and Vass<sup>2</sup> as follows:

1. Composition tumors in which both the parenchyma and stroma have become malignant.
2. Combination tumors in which two different growths develop from a single stem cell.
3. Collision tumors in which two independent tumors are present and mutually invade each other.

Many of the tumors so reported fall into the first two types in which both elements are intimately mixed. Many of these have been shown to be markedly undifferentiated carcinomas giving the appearance of sarcomas.<sup>2,3</sup> The sarcomatous parts of other tumors are thought to represent benign changes in the

supporting stroma giving the appearance of a sarcoma but without the ability to metastasize



Fig 5 A a f m i t s with lymph od Th lymph  
od t uctur app ar at th pp ight whil th th ken d cap ul  
at th l ft Th f f m rra g ment of the t s b tw en c n b en  
( $\times 100$ )

Lane recently reported a series of 10 cases similar to the one presented here. They were large polypoid sarcomatous growths associated with an adjacent carcinoma. It was his opinion that the sarcomatous elements were benign, reactive changes in the stroma without the ability to metastasize. The term pseudosarcoma was thus applied to these growths. Although the present case is very similar to those reported by Lane it is of some interest in that a frank metastatic sarcomatous lesion was identified in a lymph node. It is true however that the squamous cell carcinoma is represented in the nodes to a much greater extent than the sarcoma. In this situation the possibility has been raised that the carcinoma which in some manner caused the development of a pseudosarcoma at the primary site may cause a similar pseudosarcomatous change in the stroma adjacent to a metastasis. The present case however is a sarcoma of muscle origin and the elements found

invading deeply into the tongue musculature and as metastases in a lymph node are of the same type. It seems more likely,



Figure 6 Photomicrograph of an area of squamous cell metastases within the lymph node ( $\times 100$ )

therefore, that this is a metastasis rather than a benign transformation of lymph node stroma.

#### SUMMARY

The case presented is an unusual form of collision tumor in which both elements have metastasized. The epithelial component is a squamous cell carcinoma. The sarcomatous elements have been shown to be of muscle origin, and show both deep invasion and distant metastases to nodes.

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**ACKNOWLEDGMENT** The authors wish to express their appreciation to Capt Robert B. Brown, MC USN, Chief of Surgery at the U. S. Naval Hospital Bethesda, Md., for his helpful suggestions relating to the preparation of this paper.

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### TREATMENT OF HEMORRHOIDAL DISEASE

In curre t m d cal l i t e r a t u r e t h e r e a r e f w a r t i c l e s o n t h e s u b j e c t o f h e m o r r h o i d c t o m y a n d t h o t h a t d o p p a r c o n n o n l y t e c h n i q u e T h e r e s e e m t o b e n o a t t e m p t s t o t r y t h e r e s u l t s o f t h e o p e r a t i o n o r t o c o m p a r e t h e e f f e c t i v e n e s s o f o p e r a t i v e t r e a t m e n t w i t h n o n o p e r a t i v e t r e a t m e n t o f t h e d i s e a s e T h e c r u c i a l q u e s t i o n i s w h e t h e r t h e p a t i e n t b e n e f i t s f o r g o o d r e a s o n s I n d i c a t i o n s f o r t h e o p e r a t i o n w h i c h a r e g i v e n i n m o d e r n t e x t b o o k s a p p e a r t o b e s u n d b u t t h e y s h o u l d o b v i o u s l y n o t b e b o a r d e d t o i n c l u d e a l l p a t i e n t s w i t h s y m p t o m a t i c h e m o r r h o i d s w h o c o m e u n d e r t h e c a r e o f a n o c c a s i o n a l s u r g e o n A n y s u r g e o n n o t m a i n t a i n i n g p r i m a r y i n t e r e s t i n p a t h o l o g y w h o d o e s

l i g e n u m b e r o f h e m o r r h o i d e c t o m i e s s a f a i r t a r g e t f o r t r e a t m e n t M a n y o f t h e p a t i e n t s w h o h a v e h e m o r r h o i d s c o u l d d o u b t l e s s b e t r e a t e d s u c c e s s f u l l y b y c o n s e r v a t i v e m e t h o d s a l o n e T h e y m a y n e e d n o t h i n g m o r e t h a n s o m e g o o d a d v i c e a b o u t p e r s o n a l h y g i e n e a n d p e r h a p s a f e w d a y s o f b e d r e s t A w a r m f u l s o a p a n d w a t e r c l a n n i n g o f t h e a n u s a f t e r e a c h b o w e l m o v e m e n t o n t l e a s t o n e d a y i s e f f e c t i v e i n c l e a r i n g t h e c h r o n i c i n f e c t i o n t h a t i s g e n e r a l l y r e c o g n i z e d a s t h e u s u a l c a u s e o f p a i n f u l h e m o r r h o i d I f t h e h e m o r r h o i d

i s l a g e t h e y s h o u l d r e s p o n d r a p i d l y w h e n t h e f a v o r a b l e h e m o d y n a m i c s p r o v i d e d b y b e d r e s t a r e a d d e d t o a r e g i m e n o f c l i n i c a l t r e a t m e n t I s i t p o s s i b l e t h a t t h e p a t i e n t t a k i n g c a r e g i v e n t o t h e s e p a t i e n t s a f t e r a h e m o r r h o i d e c t o m y i n o r d e r t o o b t a i n a p e r m a n e n t c u r e w o u l d c u r e m o s t o f t h e m e v e n w i t h o u t a n o p e r a t i v e p r o c e d u r e A c o m p a r i s o n o f t h i s c o u r s e o f t h e r a p y w i t h t h e c o n s e r v a t i v e t r e a t m e n t w o u l d d o u b t l e b e e n l i g h t e n i n g

—F JOHN LEWIS

*Surgery*

p 431 A g t 1958

# Perforated Meckel's Diverticulum in a Three Month Old Infant

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GILBERT F MUELLER *Captain USAF (MC)*

IT IS well known that Meckel's diverticulum can give rise to serious complications, especially when it becomes manifest in the pediatric age group. A case is described to illustrate the serious nature of these complications in the infant, and discusses briefly the clinicopathologic picture.

## CASE REPORT

A 3 month old infant was seen in September 1957 at this hospital because of blood in the stools. He was in good health until the day of admission when the mother noticed three stools containing blood. One of the stools consisted almost entirely of dark blood. Others were dark blood mixed with stool. The infant was asymptomatic and appeared happy. There was no history of vomiting, loose stools, or episodes of crying.

Initial physical examination revealed a healthy appearing infant without pallor and in no apparent distress. His rectal temperature was 100.4 F. Results of examination of the abdomen were negative. Rectal examination revealed formed stool mixed with dark blood.

Admission laboratory tests revealed a white blood cell count of 13,300 per  $\mu$ l with 31 per cent neutrophils, 2 per cent band forms, 64 per cent lymphocytes, and 3 per cent eosinophils. Hemoglobin was 9.8 grams. Urinalysis was negative.

A flat roentgenogram of the abdomen showed no abnormality. A tentative diagnosis of Meckel's diverticulum or intestinal polyp was made.

The following morning while being examined the infant suddenly began to scream as if he were in pain and flexed his legs on his abdomen periodically. The abdominal findings changed. There was muscle spasm and apparent tenderness to palpation in the right periumbilical area. No definite mass was palpable. A barium enema was given. The barium flowed to the cecum without delay or obstruction. However, despite attempts with increased hydrostatic pressure and

p l pation the terminal ileum could not be filled The small bowel was not distended A repeat white blood cell count showed 20 000 per  $\mu$ l with 87 per cent neutrophils Further roentgenograms prior to surgical intervention revealed small bowel distention and an oval collection of barium in the cecum with definite concave border suggestive of an ileocecal intussusception

Abdominal exploration through a right ectus inc on 12 hours after the onset of acute abdominal symptoms revealed a localized area in the ileal region containing sero sanguineous fluid which was not foul smelling and the omentum adherent to an acutely inflamed 1.5 cm Meckel's diverticulum There was no evidence of an intussusception Removal of the omentum revealed a necrotic perforated ulcer at the base of the diverticulum measuring 2 mm in diameter A yellowish fluid exuded from the perforation suggestive of gastric secretion The diverticulum was clamped at its base and removed The appendix was not seen or searched for Penicillin and streptomycin sulfate were installed into the abdominal cavity and the abdomen was closed A subcutaneous drain was left in place Postoperatively the infant was placed on high dosage of antibiotics and his temperature returned to normal on the second day Oral feeding was instituted on the third day and he was discharged the 12th day after surgery

Histopathologic examination revealed the presence of acute inflammatory changes with perforation at the base of the diverticulum Gastric mucosa was demonstrated in the wall of the diverticulum

### DISCUSSION

In addition to the normal intestinal mucosa a diverticulum may contain heterotopic gastric mucosa pancreatic tissue or duodenal glands (Brunner's glands) either in the wall or in the form of polypoid accumulations of these tissues 25 per cent of all Meckel's diverticuli contain heterotopic tissue most often gastric in type The gastric tissues are capable of secreting hydrochloric acid and pepsin The secretion usually begins synchronously with the gastric activity Thus all mucosa like structures in the diverticulum are exposed to these digestive juices at a time when food and intestinal juices are not present to act as buffers

Three distinct types of pathologic changes may occur when a Meckel's diverticulum is present producing three main groups of symptom complexes (1) ulceration with or without perforation (2) infection resulting in diverticulitis and (3) intestinal obstruction In addition fistula formation which must be differentiated from a patent urachus and rare tumors can occur

First ulceration with or without perforation Heterotopic gastric mucosa is of paramount importance for as it is capable of producing hydrochloric acid and pepsin it is responsible for the

peptic ulceration that occurs in such cases. The ulcers are commonly observed at the base of the diverticulum and may produce perforation, hemorrhage, or both. This case is an illustration in point for the facts stated above. That hemorrhage and perforation occurred within three months of the birth of this infant attests to the susceptibility of the ileal mucosa when exposed to gastric secretions, unbuffered by food, biliary and pancreatic juices. When bleeding occurs, nearly 100 per cent of the specimens probably will show gastric mucosa on careful examination, according to Berman, Schneider, and Potts.<sup>2</sup> Gastric mucosa was demonstrated in the microscopic analysis of the diverticulum in this case. The hemorrhage, without associated abdominal pain, is typical of a Meckel's diverticulum, and is the single most common finding.<sup>3</sup> The occurrence of rectal bleeding, greater in amount than usually seen with polyps or fissures, plus the dark color and the fact that blood is mixed with stool, is the usual finding. The absence of mucoid material, which causes jelly-like or currant-jelly stool, is another helpful point to differentiate a Meckel's diverticulum from intussusception.

Second, infection resulting from diverticulitis. Meckel's diverticulum may be the seat of inflammatory changes which may be acute or chronic and may closely simulate acute appendicitis.<sup>4</sup> Perforation may occur, but is nearly always caused by the presence of gangrene in the diverticulum. When perforation results from peptic disease, gangrene is absent.

Third, obstruction. Meckel's diverticulum may be the cause of intestinal obstruction. It may act as an axis about which loops of bowels rotate to form a volvulus. Or it may be followed by a band that adheres to any peritoneal surface, forming an opening through which many various forms of intestinal strangulation may take place. On the other hand, Meckel's diverticulum may be the leading point of an intussusception.

#### SUMMARY

A single case of Meckel's diverticulum, with hemorrhage and perforation, in a 3-month-old infant, with successful treatment, is presented, followed by a brief discussion.

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# The Fate of Bone Graft Replacement in Monostotic Paget's Disease

H TODD STRADFORD C pt MC USN

**P**AGET'S DISEASE of bone (osteitis deformans) is described in the literature frequently but there are few reports on the surgical treatment and even a greater paucity in regard to the fate of bone grafts. In 1918 Abbe reported surgical repair of a grossly deformed maxilla with excellent healing and restoration of function. In his article there is a photograph of a tibia deformed by monostotic Paget's disease. He may have been suggesting surgical repair but he makes no mention of this idea in his article. In reviewing the literature Kanavel (in 1907) and New and Harper (in 1933) found that at frequent intervals surgical intervention had been advocated in cases of Paget's disease of facial bones. The opposite has been true in bones of the extremities.

*Trinca of Australia and Brocq Layani and Thoyer Rozart of France* recommended correction of deformities by osteotomy. Amputation was suggested by Charbonnel and Doche in the French literature and by Wanke in the German literature. This was mainly for malignancy. Stein suggested osteotomy as the treatment of choice but admitted that the deformities and disease continue.

This case presents the fate of a bone graft in a patient with proven Paget's disease. I do not advocate this method of treatment for all deforming Paget's disease but where a deforming monostotic lesion presents it offers more than a transitory osteotomy.

## CASE REPORT

In December 1948 19 year old man was referred to the orthopedic service of a naval hospital because of a painful left forearm of 4 years duration. Onset had been insidious. The forearm had gradually become bowed on the distal side. Past history revealed that in 1946 the patient had been admitted to the hospital because of severe pain of 6 months duration. A biopsy had been performed at that time but no specific diagnosis had been made.

F m U S N 1 H p l B h d Md C pt Str df d w gn d Arm d  
F I tu f P th l gy W h g D C.

Roentgenograms on 11 January 1949 revealed a grossly deformed bone with a moth eaten appearance but without loss of cortical integrity (fig 1) Laboratory studies revealed normal findings, with calcium and phosphorus within normal limits alkaline phosphatase ranged from 6 to 9.4 Bodansky units



*Fig 1 Monostotic Paget's disease of four years duration.*

A biopsy revealed typical Paget's disease. Roentgenographic survey of the skeleton failed to reveal any additional foci. Because of the patient's pain and the apparent monostotic nature of the disease it was decided to excise the affected portion of the radius and replace it with a graft.

The only previous bone graft in a similarly affected bone had been a small onlay graft in the treatment of a fracture which became incorporated into the parent bone and also was affected by the disease. This case was an opportunity to determine if a major graft might escape this fate. Consequently a tibial cortical graft was chosen because its replacement would entail complete reorganization.

Through a Henry's approach the radius (fig 2) was excised from above the bicipital tubercle to within 2 cm of the wrist joint. The autogenous graft was slotted and mortised into place (fig 3) and no internal fixation other than soft tissue closure was utilized. The stability was tested by lifting the arm from the table by the graft.

The patient did well and after a convalescence of six months returned to duty. In the next 10-year period he was seen periodically. Roentgenograms made 5 years postoperatively showed the cortical graft completely reorganized with a medullary canal. In spite of Paget's disease continuing in the parts of the radius remaining from the original bone the graft had remained unaffected. General roentgeno-

graphic recheck in a 10 year follow up however revealed some revision of the graft from the end abutting onto the old bone affected by Paget's disease (fig 4) There are also changes in the lumbar

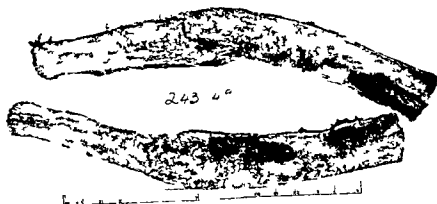


Fig 2. Tibia excised and sawed half longitudinally

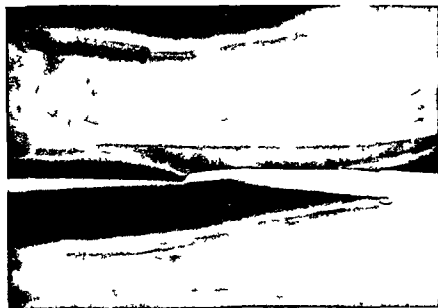


Fig 3. Intraoperative top and bottom roentgenograms showing graft placement

vertebrae and femurs. The ulna which protruded into the wrist was intended to be resected at a later date allowing biopsy of the radius and graft but the arm has remained asymptomatic and the patient

now, a Chief Petty Officer on active duty is satisfied with his wrist without further treatment

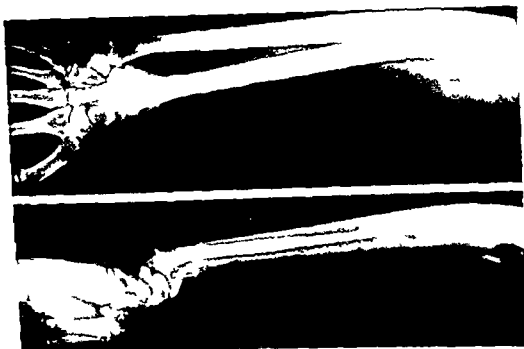


Figure 4 Radiographs 10th year following surgery showing the graft completely reorganized. Note reformation of medullary canal. Paget's disease persists in old bone left at wrist. Slight extension of the graft is considered to be by direct extension from the old remaining focus.

### SUMMARY AND CONCLUSIONS

The point of interest in the case presented is the fact that an autogenous cortical graft used to replace a radius affected by Paget's disease survived in normal function for 10 years. The graft was completely replaced and reorganized to develop a medullary canal. The portion of the graft with involvement is obviously invading from a known focus. This suggests that whatever causes Paget's disease is inherently within the affected bone, and by excision of the affected bone, the disease is eliminated for a time locally. This points negatively to a systemic origin for Paget's disease. This case reveals the need for more experimental work on this disease. Early surgical intervention in long bone deformities that are proceeding rapidly is worthy of consideration.

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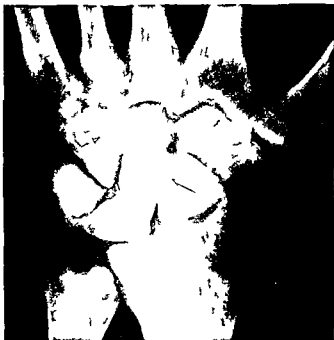


Fig 2 (a) 1) Roentgenogram showing fracture of the scaphoid. (b) 2) Roentgenogram showing fracture of the scaphoid.

### CASE REPORTS

C 1 A 20 year old patient on appointment was injured in May 1956 when he tripped over a ladder and fell on his outstretched left wrist. Following the fall he noted some weakness of his left hand and limitation of palmar flexion. On 19 November 1957 he again fell and injured his left wrist. Roentgenograms at this time showed fracture of the scaphoid and hamate bones (fig 1). The scaphoid fracture appeared to be an old injury as there was some sclerosis around the fracture site. A navicular type of fracture of the scaphoid was present three months later, the end of which roentgenogram revealed the fracture displaced to be healed (fig 2). The patient with no physical therapy and regained a normal range of wrist motion.

C 2 A 20 year old male recruit injured his right wrist February 1957 by falling from a platform. Initial roentgenogram showed a fracture of the navicular and fracture of the capitate with the proximal fragment rotated 180 degrees (fig 3). The patient was treated with a navicular type of short arm cast for eight months. Roentgenograms taken at this time revealed that the fractured navicular to be healed. The proximal position of the fractured capitate was still rotated 180 degrees (fig 4).

The patient was then treated with physical therapy and at this time of return to duty motion of the wrist was follows: var flexion

50° dorsiflexion 35° ulnar deviation 35° and radial deviation 35°  
The wrist was asymptomatic



*Figure 3 (case 2) Roentgenogram showing fractures of navicular and capitate bones with proximal fragment of capitate rotated 180°*

#### DISCUSSION

The treatment of fractures across the waist of the capitate was described by Speed as consisting of immobilization of the forearm and hand in straight extension for four weeks. Inasmuch as the patient in case 1 appeared to have an old fracture immobilization was continued until union was complete and the patient had a satisfactory result. Treatment of fractures involving rotation of the proximal portion of the capitate was described by Fenton and Rosen<sup>2</sup> as excision of the rotated fragment. It was their opinion that this was necessary.

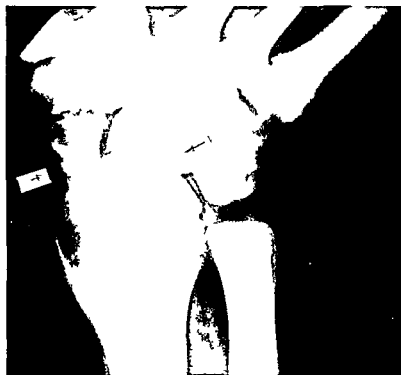


Fig 4 ( 2) R t g g m b u g b l d f tur of c l  
bo P m l p t f apt t ill t t d 180

it was avascular Jones recently reported a case treated by immobilization in which the fracture healed with the proximal fragment rotated 180°. In case 2 the patient's wrist was asymptomatic and excision of the proximal fragment was deferred. There was some indication that the rotated fragment of the capitate had become adherent to the navicular.

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37 B 146-147 F b 1955

## U S AIR FORCE NATIONAL CONSULTANTS, COMMAND SURGEONS MEET AT ANDREWS AFB

The annual conference of the Air Force command surgeons and national consultants to the Surgeon General was held during the first week of September in the new hospital at Andrews Air Force Base near Washington D C This three day meeting according to Major General Dan C Ogle USAF (MC) Surgeon General of the Air Force provides an interchange of the latest military and civilian medical thinking and technics It is a part of the program of the Air Force Medical Service to ensure the best possible professional care in hospitals and dispensaries



*Shown above are the staff surgeons of the Air Force Commands in the United States and overseas. Below is the group of national consultants in the various medical and surgical specialties.*





## CAPT AVERY TO HEAD MEND PROGRAM

Captain Bennett F Avery MC USN editor of the *Journal of the Medical Association* since 1 July 1955 has been appointed national coordinator of the Medical Education for National Defense (MEND) program. He has been succeeded by Colonel Robert J. Bedford USAF (MC) associate editor for the past 16 months.

Formerly dean of Boston University School of Medicine, Dr Avery has held important medical posts in the Near East. He served as professor of anatomy and later acting dean of the medical school of the American University in Beirut and from 1944 to 1949 was first Deputy General and then Advisor to the Imperial Iranian Ministry of Health. His MEND offices will remain in the Navy Bureau of Medical and Surgery where he has also held the position of chief of the publications division since 1952. His successor in that position is Captain Leslie B. Marshall MC USN (Ret).



Capt Avery

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## Medical Civil Defense Emblem

A medical civil defense emblem for worldwide use has been proposed by a committee of representatives of the World Medical Association, the International Committee of the Red Cross, and the International Committee of Military Medicine and Pharmacy. Its adoption by all countries will aid in the protection of medical personnel and equipment engaged in civil defense according to Dr Louis H. Bauer, secretary general of the WMA. The emblem is red on a white background.



The emblem

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## Tripler Army Hospital Anniversary

Tripler U.S. Army Hospital in Manila, P.H., marked its 10th anniversary of service on 10 September with a simple commemorative ceremony. The present 1,500-bed hospital under the command of Brigadier General Jack W. Schwartz MC USA replaced a former hospital built in 1906, later named Tripler General Hospital after Brigadier General Charles S. Tripler, medical director of the Army of the Potomac in the Civil War.

# OFFICERS CERTIFIED BY SPECIALTY BOARDS

## Supplementary Listing

The Surgeons General of the military medical services have announced that the following, regular Medical Corps officers have been certified by the boards indicated since the listings published in previous issues of the *Journal*

### American Board of Pediatrics

James R. Upp, Capt. USAF

### American Board of Obstetrics and Gynecology

Paul H. Strig, Maj. USAF

### American Board of Pathology

#### *Pathologic Anatomy*

Edward S. Beina, Maj. USAF

James R. Cley, Capt. USAF

William E. Cowell, Lt. USN

Robert F. Filice, Maj. USAF

Dwight B. Rulon, Comdr. USN

Clifford A. West, Maj. USA

#### *Clinical Pathology*

William W. Ayer, Capt. USN

Edward S. Beina, Maj. USAF

James R. Cley, Capt. USAF

Robert M. Dimmette, Comdr. USN

Dwight B. Rulon, Comdr. USN

### American Board of Ophthalmology

Raymond B. Lytle, Jr., Capt. USAF

Herold D. Eitzler, Jr., Lt. USN

Walter A. Furfur, Jr., Capt. USAF

Lawrence O. Cahana, Capt. USAF

Victor M. Oht, Capt. USAF

James I. Thorn, Comdr. USN

### American Board of Surgery

Walter H. Brune, Maj. USA

Richard H. Hood, Jr., Maj. USAF

Henry P. Raymond, Jr., Capt. USAF

Charles F. Reynolds, Lt. Col. USAF

### American Board of Neurological Surgery

Ernest J. Peck, Lt. Comdr. USN

### American Board of Physical Medicine and Rehabilitation

John L. Rith, Maj. USA

### American Board of Preventive Medicine

#### *Aviation Medicine*

Richard M. Felt, Lt. Col. USAF

Oliver A. May, Lt. Col. USAF

Gordon H. Rhoads, Col. USAF

John R. Troell, Lt. Col. USAF

#### *Occupational Medicine*

Dwight H. Herber, Capt. USN

The inclusion of roentgenograms and angiocardiographs would have improved the section on congenital heart disease

This reviewer is impressed with the fund of information in this volume. Some infrequently encountered disease conditions rarely mentioned in other textbooks of pathology are included here and given due attention. Frequently short bibliography sketches of important figures in the field as well as an explanation of the derivation of many of the terms used in pathology add much to the interest of the reader. The number of references is large. The two volumes of this first course can be considered typical should they be deserved place among the better and more useful textbooks of pathology.

—WILLIAM M. SILLIPHANT Captain MC USN

FUNCTIONAL BRACING OF THE UPPER EXTREMITIES edited by Rymond E. S. L. W. T. D. L. T. T. D. by M. L. H. A. D. Ed. D. F. W. D. by C. B. L. O. B. H. L. M. D. 463 pages. Illustrated. Chicago: C. Th. M. P. B. L. H. Sp. Ing. L. D. Ill. 1958. P. \$9.50.

This informative book is an outgrowth of a training program sponsored by the Physiotherapy Research Board of the National Academy of Sciences and was written to enable a more general dissemination of the rationale, technique and principles involved in the prescribing, manufacture and fitting of upper extremity functional braces to individuals suffering from some degree of upper extremity paralysis. There are chapters on the functional anatomy of the hand, basic and functional anatomy of the arm and shoulder, the biomechanics of functional hand plants and arm braces, and nonfunctional assistive hand splint, feeding devices, special sensitive devices of many varieties such as swivel pen, comb and razor holders and page turners for use on a T-bar, etc. This book is of value to the pediatric residents, surgeons, orthotists, prosthetists, occupational therapists, physical therapists, physicians and rehabilitation specialists. As all are members of any well organized rehabilitative team for the care of disabled patients, they should all understand their place in the program and the importance and relationship of their work to that of all the other members of the team. Such understanding will automatically result when any intelligent person reads this book. Highly recommended for all. —DAVID C. KELLSEY Lieutenant Colonel USAF (MC)

ROENTGENOLOGY OF THE CHEST edited by C. L. M. B. R. B. M. D. F. C. C. P. 484 pages. Illustrated. Chicago: C. Th. M. P. B. L. H. Sp. Ing. L. D. Ill. 1958. P. \$19.50.

The stated purpose of this book is to present roentgenology of the chest to the radiologist from the clinical standpoint and to the clinician from the radiologist's viewpoint. This bilateral approach to the problem of disease of the heart and lungs is unique and the end result is excellent. The pre-technique of physiology, anatomy and surgery are written by leading experts on their own principles. An outstanding example of this bilateral approach is the chapter on Special Signs in Roentgenology. This will aid the clinician in understanding the specific meaning of findings on the chest x-ray. Understanding the

signs aids the evaluation of chest films and is the difference between intelligent interpretation of the roentgenograms and pure guesswork which depends upon a good memory of previous case material. On the other hand for the radiologist there is a chapter on physiologic considerations of intra alveolar pressure. This type of information will improve his ability to get the maximum information obtainable from a chest film. All of the major and many of the rare chest diseases are very adequately covered. This is considered to be the most complete yet concise highly readable textbook on chest disease available. It would be a most valuable addition to the library of anyone involved with chest disease or chest roentgenology.

—JAMES M. KEEGAN Lt Col USAF (MC)

DISEASES OF THE ESOPHAGUS by J Terracol and Richard H Sweet.  
682 page illustrated W B Saunders Company Philadelphia Pa  
1958 Price \$20

This is the first American edition of a book which appeared originally in French for the first two editions. This is an ideal volume for all physicians interested in the diseases of the esophagus. The sections on anatomy physiology and normal roentgen examination of the esophagus are outstanding. The operative procedures are explained in great detail. The indications and contraindications for esophagoscopy and other instrumental exploration are covered completely. The organization of the various afflictions of the esophagus by chapters makes this a ready reference book with information easily available. Every condition that might occur to or in the esophagus is covered completely. The appendix contains diets and tube feedings for patients with esophageal diseases. The bibliography for the second French edition is included in its entirety but the bibliography for the first edition is not included. The majority of the references are in foreign literature but the material pertaining to recent advances in the treatment and diagnosis of diseases of the esophagus in the American literature is included. All of the illustrations are clear and more than adequate for a complete understanding of the condition discussed. This book is recommended for the library of all military hospitals and also for any physician who is interested in diseases of the esophagus whether from a surgical or internal medical standpoint. The operative descriptions would be very valuable to the chest surgeons.

—EDWARD P M LARNEY MC USN

ADVANCES IN INTERNAL MEDICINE edited by William Dock, M D and  
I Snapper M D Volume IX 311 page illustrated The Year Book  
Publishers Inc Chicago Ill 1958 Price \$8 50

The editors of this annual volume each year select eight to ten topics of importance in internal medicine for review. The subjects cover areas of general interest wherein recent advances have made an up-to-date review of particular value. Each section is written by a recognized authority in that field. The areas covered this year are vitamin B<sub>12</sub> metabolism corticosteroids and infections hyperparathyroidism hereditary defects in clotting mechanisms pathogenesis

of glom ulonephr t s pathophysiology of carcinoid tumors and renal tubular function The discussio s are well and carefully written include numerous references and give clear concise summary f the background and current status in that field The volume has an author and subject index which add to its value The indexing and extensive bibliography make it a valuable source of references to other articles in the literature It is highly recommended

—CHRISTIAN GRONBECK, J. L. C. I. MC USA

A MANUAL ON CARDIAC RESUSCITATION by Rbert M H I M D F A  
C S 2d d t 208 p g 11 tr t d Ch I C Th m P bl h  
Sp g f ld Ill 1958 Pr \$5 50

This is the second edition of a well written manual The value of proper management of cardiac arrest is stressed throughout and responsibility to meet the emergency is placed squarely on the shoulders of every physician who attempts surgery Much research and thought has gone into the compilation of this manual Application of cardiac resuscitation has been extended beyond the surgeon and operating room indications for thoracotomy and cardiac massage are broadened Dr Hosler suggests and proves that at times our conception of death is reversible He cites the work of Yater who found in 1950 a topsy of men who died of coronary artery disease that one third showed no evidence of myocardial damage This suggests that many of the cases might have been saved if cardiac resuscitation had been available The use of a doctor so resuscitated is cited Recognition and treatment of cardiac arrest with or without ventricular fibrillation are carefully outlined Stresses placed on re-establishment of the oxygen system and restoration of the heart beat Every required instrument and drug is described The technique of massage and many of the instruments are illustrated by photograph or drawing The contents of this book should be known to all anesthesiologists and to all surgeons regardless of subspecialty It should be in the library of all hospitals and a part of the resuscitation kit of all emergency departments operating rooms The material also should be taught in every medical school —LUTHER G BELL, C. P. MC USN

A THERAPY FOR ANXIETY TENSION REACTIONS by Gerb d B. H g  
M D H nry H D x M D d H rm A D k I M D 110 p g  
Th M m ll C N w Y k N Y 1958 P \$3 50

Over twenty years ago Edmund Jacobson at the University of Chicago described a controversial type of therapy for treating chronic anxiety tension states In this monograph written by three psychiatrists from the University of Oregon for nonpsychiatric physicians a modification or short cut in the Jacobson method is described The basis of this therapy is that the tension habit The chronically tensioned person has practiced tension largely by imitation and the tension habit is formed Muscle tension comes first anxiety follows as a part of general habituation The habit can be changed like any other habit Anxiety will persist as long as tension is present This book describes the method of changing the habit of tension First the patient learns



in lieu thereof  
for patients and

direct observations by the individual authors  
fracture ward

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but the ability to differentiate the self from the  
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confusion of his personal identity and the  
portion of the book presenting interesting  
and interpretations in support of the basic

Two chapters  
a chronology  
of schizophrenia  
chronic schizo-  
phrenia

related to the theory of mental functioning with  
most of the various psychopathologic theories  
is an excellent chapter on the treatment of  
in a therapeutic environment followed by a  
conclusion to make a fitting ending to this book

In my opinion  
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author are to be congratulated for an excellent  
much neglected group of patients. This work  
and value to psychiatrists and related workers  
the analytic study of mental illness. Others  
because it provides a clear picture of the  
schizophrenics. I can't help but think that  
the last studies of chronic schizophrenia from  
a viewpoint because the current influence of  
emphasis on the chemophysiological aspects of  
dominate the trend of investigational studies

This book describes

in any well rounded library on psychoses

—STEPHEN MOURAT, L.C.I. MC USA

MEDICAL EMERGENCIES  
M. D. F.  
M. P.  
Comp. y. f.

Edited by F. C. D. Murphy  
and A. T. Ath. F. W. D. by G. S.  
H. E. T. 635 p. g. Ill. st. ed. F. A. D.  
P. 1958

This is the first edition of a well known practical book on the  
diagnosis and treatment of medical emergencies. Major revisions  
have been made in chapters dealing with the collagen diseases, acute  
renal failure, liver diseases, and antibiotic therapy of acute infections.  
The most recent trends in the treatment and prevention of rheumatic  
fever are succinctly presented. However, not all regimens for the  
treatment of other collagen diseases are given.

Though a clear and comprehensive table of the differential diagnosis  
of acute glomerulonephritis and acute toxic nephrosis (lower nephron  
nephrosis or acute renal failure) is given, certain details of treatment  
presented are either controversial (e.g., three days of serum albumin  
given intravenously for the former) or not clearly spelled out (e.g.,  
types and quantity ranges of parenteral fluid recommended for the  
latter).

Occasionally the primary aim of conciseness is somewhat impaired by inclusion of diseases that are not strictly emergencies (e g certain chronic anemias) In other places reference to certain theories is made Interesting as these may be it is believed that at least some of the space devoted to them could profitably be devoted to more detail on appropriate topics

The revised section on diseases of the liver is superb for its concise yet comprehensive account of the pathophysiology differential diagnosis precise interpretation of laboratory tests and illustrations of physical examination technics as well as treatment

The appendix on chemotherapy of the common bacterial infections furnishes a practical and ready reference to drugs for certain bacteria and their efficacy according to recently compiled percentages This permits the best selection before results of sensitivity tests are available

This volume is heartily recommended to medical students interns residents and general practitioners

—H LEONARD JONES Jr Capt MC USN

THE BRAIN AND HUMAN BEHAVIOR Proceedings of the Association for Research In Nervous and Mental Disease December 7 and 8 1956 New York N Y Editors Harry C Solomon M D Stanley Cobb M D and Wilder Penfield M D 564 pages with 200 illustrations and 53 tables The Williams & Wilkins Co Baltimore Md 1958 Price \$15

This is the thirty sixth in a series of annual symposia each devoted to a subject of current interest The current topic is discussed by an imposing group of neurologists psychiatrists neurophysiologists pharmacologists chemists anatomists psychologists and neurosurgeons Like many of its predecessors the book is well bound clearly printed expensive and dull An avalanche of words effectively reduces reader interest This reviewer searched for clear simply expressed ideas but found few The best papers are short but unfortunately few in number This reviewer found the book hard to finish No real definition of The Brain and Human Behavior appeared Much speculation free association and philosophical meandering obscure what facts are available An index of sorts plus a list of the association's membership completes the book It is too expensive and too long for any but those with an excess of time and a lively interest in this important topic to enjoy —HENRY W HOGAN Maj MC USA

CLINICAL OBSTETRICS AND GYNECOLOGY Volume 1 Number 1 A quarterly book series Symposium on Medical Problems in Pregnancy edited by Curtis J Lund M D Symposium on Management of Endocrine Problems edited by Allan C Bruns M D 288 pages illustrated Paul B Hoeber Inc Medical Book Department of Harper & Brothers New York N Y March 1958 Price \$18 for four consecutive numbers

The section on medical problems in pregnancy was not intended to replace the works of other specialists but to present the point of view of specialists on the common medical complications so important in



the morbid ty and mortality of pregnancy. In the first chapter on anemia in pregnancy a brief history of the advance of this problem in obstetrics plus a classification of anemia in pregnancy and its treatment is given. This subject is then concluded with an excellent summary on the factors introduced by pregnancy which singly or in combination produce anemia. A word of caution about whole blood transfusion is not being the treatment of choice for any common pregnancy anemia is an important one. In addition prevention is a duty of the physician to his patient. The section on management of endocrine problems begins with diagnostic aids for endocrine management. The fact is emphasized that none of the various forms of therapy ranging from diet to various hormones has stood the test of time in the treatment of dysfunctional uterine bleeding. Most important is proper diagnosis and intermittent progesterone therapy. The Menopause by D. Barne emphasizes the need for accuracy rather than casual diagnosis with the need for actual laboratory procedures being necessary only in the case of possible premature menopause occurring in the thirties or earlier. Other sections of the text deal with the endocrine treatment of fertility followed by threatened and habitual abortion, management of diabetes and pregnancy problems related to growth and sexual development, the adrenogenital syndrome, adrenal hyperplasia and pseudo-Cushing's syndrome, and the adrenal gland. This text is a concise review of the previously treated problems with an up-to-date bibliography of each subject. It is of definite interest and value to the specialist in this field.

—HUMBERT L. RIVA, C. L. MC USA

THE MANAGEMENT OF CHILDHOOD ASTHMA by F. d. Sp. M. D.  
116 p. g. ll. t. d. Charl. C. Th. m. P. bl. h. Sp. g. f. ld.  
Ill. 1958. P. \$4.75

This is an excellent concise book on a disease important to the general practitioner and the pediatrician. The author has condensed his presentation but adequately covered his subject.

Treatment of childhood asthma varies regionally according to local problems such as climate, allergen, etc. etc. etc. While the author has undoubtedly been influenced by his experiences in Kansas, most of his suggestions are applicable throughout the country. Little is said about the psychosocial factors in aggravating the disease. His emphasis upon a careful history and the establishment of good rapport with the parents is especially to be commended. This is a practical and thoughtful book and a welcome addition to the medical literature on this subject. —JOHN F. SHAUL, Capt. MC USN

ANOMALIES OF INFANTS AND CHILDREN by D. M. C. H. g. b. Mayer, D. D.  
S. M. D. F. A. C. S. F. I. C. S. and W. I. A. Swank, M. D.  
F. A. C. S. F. I. C. S. 454 p. g. ll. t. d. Th. Blak. D.  
M. G. W. H. ll. B. k. C. mp. y. In. N. w. Y. k. N. Y. 1958. P. \$12

This book is just what it is stated to be written primarily for the student and general practitioner. As such it does an extremely fine job of covering congenital and acquired anomalies of children from a general point of view. The contents are subdivided into specific areas

for easy reference and the index is good for easy location of specific anomalies both of which make for ready access to the user

The various entities are broken down and discussed as to definition etiology diagnosis prognosis and treatment The embryology sections are good for this type of book but the treatment sections could be a bit more specific in certain cases The etiology section would be excellent for the parents of deformed children to read as explanations for their many doubts and questions Two or three of the classifications of anomalies in this book are new and not in keeping with those of general usage I do not believe that further confusion of the medical nomenclature is indicated

This book is excellent for the medical student intern and young resident in many of the specialties and can serve as a ready reference book for a quick bird's eye view of a specific entity in this field The last chapter "Accidents to Children" should be read and absorbed by everyone It is a giant step in the right direction that of preventive medicine to which we all should pay more attention

—HAL B JENNINGS Jr Lt Col MC USA

**ELECTROCARDIOGRAM CLINICS** by Joseph E F Riseman M D and Elliot L Sagall M D Clinic I The Diagnosis and Treatment of Angina Pectoris Clinic II The Role of the Electrocardiogram in Establishing the Diagnosis of Acute Myocardial Infarction Clinic III Problems in the Diagnosis of Acute Myocardial Infarction Clinic IV The Role of the Electrocardiogram in the Diagnosis of Pulmonary Embolism 259 pages illustrated The McGraw-Hill Company New York N Y 1958 Price \$10.50

This book covers only one small aspect of electrocardiography It deals with the electrocardiographic tracings found in patients with coronary artery disease angina pectoris and myocardial infarction The text is a series of electrocardiograms of patients with clinical history and physical findings and other pertinent clinical data After a brief presentation of the clinical aspects the electrocardiogram is interpreted and the case is discussed in a question and answer manner While the concept of presenting electrocardiogram clinics is good it is unfortunate that the authors have restricted their interpretations to old style pattern terminology Each electrocardiogram is interpreted by groups of leads beginning with the standard lead the augmented limb leads and finally the unipolar precordial leads After this descriptive terminology the final interpretation is made Most interpretations of each electrocardiogram occupy a full printed page One wonders if the authors are familiar with the relationship of the augmented limb leads to the bipolar standard leads and the use of modern vector concepts The reader who is interested in concise modern electrocardiographic principles will not find them in this text It is open to criticism on a number of the clinical interpretations and inferences which are made and presents no new facets in the field of electrocardiography —LAWRENCE LAMB M D

A TEXTBOOK OF ORAL PATHOLOGY by William G. Shafer, B. S., D. D. S.,  
 M. S., M. y. d. A. H. D. D. S., M. S., d. B. m. t. M. L. y. A. B.  
 D. D. S., M. S. 714 p. g. ll. t. t. d. W. B. Sa. d. C. mp. y. Ph. l.  
 d. lph. Pa. 1958 P. \$15

The most marked favorable feature of this text is the clarity of presentation of material. Each subject and lesion is discussed in terms of its clinical features, histologic features, and treatment and prognosis. Of great value as a teaching text for undergraduate dental students is the thorough and modern coverage given to dental caries, diseases of the pulp and peripical tissues, and periodontal disease. These areas represent the bulk of the problems facing the average general practicing dentist. A few specific criticisms are worthy of note. In the discussion of fissural or developmental cyst, no mention is made of the median mandibular cysts. The problem of the oral leukoplakias and the need for separation from leukoplakia is well discussed. However, the illustrations offered are so small that the important feature of dyskeratosis cannot be visualized. These omissions detract from the value of such a discussion. It appears to be of questionable value to include the radicular cyst with the odontogenic tumors, notwithstanding the author's introductory statement concerning involvement of similar tissues. Traditionally, and on a basis of clarity and continuity, better established by inclusion with parodontal lesions. This text is highly recommended for use in teaching oral pathology to dental students, to dental specialists, and to general practitioners of dentistry who desire a firm foundation in oral pathology.

—WILLIAM G. SPRAGUE, Maj, USAF (DC)

CLINICAL PERIODONTOLOGY, Th. P.odontum, H. lth. d. D.  
 (R. gn. d. gn. d. r. tm. t. f. p. odont. l. d. th.  
 practi. of gener. l. d. t. try) by Irv. g. Gl. kman, B. S., D. M. D.,  
 F. A. C. D. 2d ed. t. on. 978 page. ll. t. t. d. w. h. 720 f. g. W. B.  
 S. und. C. mp. y. Ph. l. d. lph. Pa. 1958 P. c. \$17.50

The appearance of a new edition makes it wonder what change have justified it. In this second edition, the whole book has been reworked, and there are changes. Greatest of these is the addition of the section on gingival plastic surgery following current philosophies of practice. Some bibliographies have been condensed, however, all classic references retained. There has been some rearranging of subject material into more homogeneous groupings and changes in sequence. The printing and format are different. The illustrations are clearer and more detailed. To those of us who have become attached to the first edition, this is an improvement, but not an obsolescence of what is probably the most comprehensive periodontal text in the English language. The author's wide experience in research, teaching, and as a practicing clinician makes the book of universal appeal to students, general practitioners, and specialists in periodontia.

Half of the book is devoted to cleared finite treatment of practical applications. The balance treats periodontal anatomy, histology, physiology, pathology, etiology, and classification. There is thorough cover

age of each subject For those interested in improving the general standards of practice here is a book which can almost be guaranteed to do so For the uninitiated it will certainly open fascinating possibilities for successful treatment —JULES D KARTMAN Lt Col USAF (MC)

PRINCIPLES OF RESEARCH IN BIOLOGY AND MEDICINE by Dwight J Igle B S M S Ph D 123 pages J B Lippincott Company Philadelphia P 1958 Price \$4 75

This small volume consists of the author's views on those problems in research which relate primarily to the philosophy of work as it is commonly undertaken in the clinical and laboratory approach to medical problems He has cleverly introduced the humor of Lewis Carroll to emphasize some of his principles

The eleven chapters cover such general subjects as limitations of mind causality probability heteropoietic factors interpretation of results and theory in biology and medicine Each of these is in itself so complex that volumes have been written on them The author's coverage of the subject is limited to principles but is some times lost because of the lack of specific examples to illustrate what the author considers important points

For those engaged in medical research the volume will provide an interesting evening's entertainment

—JAMES B HARTGERING Lt Col MC USA

ELECTROCARDIOGRAPHIC ANALYSIS Volume I Biophysical Principles of Electrocardiography by Robert H Bayley M D 237 pages illustrated, Paul B Hoeber Inc Medical Book Department of Harper & Brothers New York N Y 1958 Price \$8

This authoritative book by a noted electrocardiologist is the first of a series Lest readers be awed by the title of this volume its forthcoming companion *Clinical Aspects of Electrocardiography* will hold more promise for the physician who is oriented toward purely clinical aspects of the subject Because the analytic method of presentation employed by the author is developed in a stepwise manner the reader must resist the strong temptation to hurry through the tedious study required to gain an understanding of concepts relating to the solid angle membrane potentials and double layer distribution because these discussions among others formulate the basis for consideration of the more appealing clinical subjects which follow It is difficult to single out any one section of this treatise for special comment It is the over all integration of the concepts presented which will provide the reader with a rational approach to an analysis of unusual electrocardiograms or difficult problems which do not fit a recognized pattern It is appropriate to indicate however that the sections devoted to the abnormalities of vector accession (depolarization) are excellent particularly with respect to the relationship of myocardial infarction and conduction disturbances One of the most valuable features of this book may be found in the chapters dealing with T-wave abnormalities the ventricular gradient and the current of injury, etc

cause much of the material offered concerning these subjects cannot be readily found elsewhere. The sections on local ventricular ischemia including the electrocardiographic changes of impending myocardial infarct are of particular interest. A comprehensive chapter on the major considerations available for those interested in this phase of the subject and the more uninitiated will find the glossary of frequently used terms of considerable assistance. This book was written for the serious students of the subject. Those who are unwilling to devote the time and effort required to master the basic concepts which are difficult to grasp will find themselves hopelessly lost. On the other hand those diligent readers who persevere and accomplish an understanding of the fundamentals will be rewarded. To this group the book can be highly recommended.

—JAMES A. ORBISON Lt Col MC USA

DISCOVERING OURSELVES A volume with Hummer and Hewitt  
by Edward A. Stecker M.D. S.D. and Kenneth E. Apple M.D.  
Sc.D. Illinois Northwestern University Press  
Chicago Illinois Third Edition 303  
pages Illustrated Thomas Mullan Company New York New York 1958  
Price \$4.75

This primer of dynamic psychology needs no introduction. Three editions and many thousands of copies over a period of 27 years attest both to its value and its success. Written by two of this country's foremost psychiatrists it manages in simple and lucid style to succeed where many more ponderous and highly technical tomes fail namely in imparting most of the basic and acceptable principles of dynamic psychiatry in simple English. The greatest need today is imparting information to others; the ability to communicate. This primer does this admirably and can be understood and enjoyed at all educational levels. It is particularly recommended to the layman, the novice psychiatrist and the military service and especially to the so-called well-trained individual who has forgotten to converse in plain English or who is called upon to train group not educationally for himself. —RICHARD R. CAMERON Col MC USA

PROGRESS IN PSYCHOTHERAPY Volume III Technical Psychology  
edited by J. L. Hillman M.D. and J. L. M. M. M.D. 324  
pages Illustrated Grune and Stratton Inc. New York New York 1958  
Price \$8.50

This volume one of a series issued yearly deals with current concepts of dynamically oriented psychotherapy and the various techniques used. The editors have done an excellent job of selecting extremely good articles written for the most part by outstanding people familiar with each technique. A small portion of the book deals with historical development in psychotherapy and is followed by large sections dealing with rationale and methods and containing some fascinating and thought provoking analogies. The authors do not spare feelings and dissecting some of the established scientific truths and revealing that their basic principles are at times far from flawless and often mutually excluding.

A sizeable section is devoted to special techniques and contains articles dealing with such a variety of subjects as military psychiatry marriage counseling the use of projective tests in psychotherapy et cetera. A pertinent portion of the book deals with psychopharmacology and calls to attention the rather sobering deficiencies of our knowledge of pharmacodynamics as it relates to biochemistry and neurophysiology. Such knowledge is imperative for the adequate understanding of the behavioral effects of drugs in man.

The book is concluded with some newsy reports of psychotherapy with specific problems as experienced in Canada Greece Latin American countries et cetera. The book is well worth reading especially for those who have completed or are far advanced in their psychiatric training. Although one may not agree with some of the ideas expressed by the over forty authors one must admit that there is no lack of thought provoking comments.

—STEPHEN MOURAT Lt Col MC, USA

**COCCIDIOIDOMYCOSIS** by Marshall J. Fiese M.D. F.A.C.P. Foreword by Charles E. Smith M.D. 253 pages illustrated Charles C. Thomas Springfield Ill. 1958 Price \$9.50

Until about 20 years ago coccidioid disease was of intimate concern only to physicians of sparsely settled endemic areas in California Arizona New Mexico Texas Mexico and Argentina who had the responsibility of treating patients with the disease. Now however nearly 700,000 acres of San Joaquin Valley land in California have been put under cultivation many thousands of acres of the Sonora Desert in Arizona have been turned into farms thousands of people have migrated into the farm lands of Central California and each year several million nonimmune people travel in and through these endemic areas some to develop symptoms after returning home. The infection has become of increasing interest to medical workers in all parts of the country and other parts of the world and it will become even more so. This scholarly monograph summarizing work done during the past 50 years and especially during the last two fruitful decades is most timely. Its content is of value to specialists in many fields because it deals competently with the history epidemiology mycology geographic distribution immunology pathogenesis clinical course prevention and treatment of a disease which fortunately usually mild and self-limiting can in its disseminated forms be most disfiguring and highly lethal. It can also play havoc in a laboratory where the fungus is not recognized as a constant danger and where due precautions therefore are not observed. Once begun the book is put aside only with difficulty until it has been read through. Research workers will find the bibliography of 968 references most helpful. As stated by Charles E. Smith M.D. in the foreword the monograph should be a major factor in making succeeding decades even more productive than the last two. The areas in which more knowledge is needed are indicated clearly.

—SIDNEY A. BRITTON Capt. MC, USN

MOULD FUNGI AND BRONCHIAL ASTHMA A Mycol g al d Clin cal  
 St dy by P J V D W // V lum I W th f w d by Pr f Dr  
 J b ma W terd jk. 213 p g ll t d. Ch rl C Thom P b-  
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The book by th h d of the Amsterdam Clinic for allergic dise es  
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—C. B WHITE Col. USAF (1C)

PSYCHIATRIC RESEARCH REPORTS OF THE AMERICAN PSYCHIATRIC  
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 H p t l f Ph l d lphia P 16-17 N 1956. 181 p g ll t t d  
 Ame P y h tr A u W h gt D C 1958 Pr \$2

This is an e cell nt add t n t a series wh ch was begun in July  
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 proces Th efer ce worth having and at a modest pr ce

—STEPHEN MOURAT LL C L MC USA

**ELECTRONIC INSTRUMENTATION FOR THE BEHAVIORAL SCIENCES** by *Clinto G. Brown Ph D* and *Rayford T. Saucer Ph D* A Monograph in The Bannerstone Division of American Lectures in Objective Psychiatry edited by *W. Horsley Gantt M D* 160 page illustrated Charles C Thomas Publisher Springfield Ill 1958 Price \$5.50

This monograph includes an introduction to the basis of electronics reviews the vacuum tube theory discusses power supplies, amplifiers oscillators and timing circuits Stimulus generators and the variety of input transducers for handling these stimuli are the subject of another chapter The chapter on test instruments reviews the principles of operation of the commonly used laboratory instruments Another is devoted to details of setting up a laboratory sources of equipment are suggested There is a chapter devoted to the theory and application of transistors A sizeable list of references is included for the reader who wishes to delve deeper Many diagrams and illustrations are used to clarify the text Investigators in experimental psychiatry and related fields will find this a useful reference manual

—ROBERT L. WILLIAMS Lt Col USAF (MC)

**CIBA FOUNDATION SYMPOSIUM ON THE CEREBROSPINAL FLUID—**  
Production Circulation and Absorption Editors for the Ciba Foundation *G. E. W. Wolstenholme O B E M A M B B Ch* and *Cecilia M. O'Connor B Sc* 335 pages 141 illustrations Little Brown and Company Boston Mass 1958 Price \$9

Among the many questions considered at this symposium were How accurate is our information about the anatomy of the pia arachnoid of the arachnoid villi of the choroid plexuses of the innervation and vascularization of these structures and of the arrangement and significance of the subarachnoid perivascular and perineuronal spaces? Do we really know where how and why the cerebrospinal fluid is produced and absorbed and is it a secretion excretion or transudate? Is the process under nervous or hormonal control are there secretory granules in the choroidal epithelium and what is the true function of the choroid plexuses? Can we explain the blood brain and blood cerebrospinal fluid barriers and their variations at different ages and in different regions? By what means and for what reason does the cerebrospinal fluid circulate? And how may all these fundamental considerations be correlated with clinicopathologic observations or utilized to determine the most rational modes of treatment? Anatomists neurologists pathologists psychiatrists pharmacologists and neurosurgeons came from all parts of the world to attend this meeting to contribute from their research and reflections The book contains 15 papers presenting careful and commendable work on the structure and function of choroid plexuses arachnoid granulations and meninges on the formation circulation and absorption of cerebrospinal fluid and on blood cerebrospinal fluid barriers The open discussions following each paper are very interesting especially the concluding one This volume is recommended for purchase by medical libraries but not by individuals

—THEODORE M. BADGLEY M J MC USA



ANNALS OF THE NEW YORK ACADEMY OF SCIENCES V 1 70 A t 3  
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The phy ci the doctor of veterinary medicin nd allied sc  
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—ROBERT R. MILLER C I USAF (VC)

THE YEAR BOOK OF PATHOLOGY AND CLINICAL PATHOLOGY (1957 1958  
 Y B k S ) d t d by W ll m B. W tm B S M D 478  
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 P \$8

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 ogist d s d nt in p thology —HOWARD A VAN AUKEN C I MC USA



- TEXTBOOK OF MICROBIOLOGY by Ken th L Burdon Ph B S M  
Ph D 4th d t 645 p g ll tr t d Th M m llan C mp y  
N w Y k N Y 1958 P \$5 75
- THE GANG A St dy t Ad l t B h by H b t A Bl h and A thur  
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- HEARING THERAPY f CHILDREN by Al St g M A W g J F t b  
M A L R y D H dg k Ph D J m W Ph l p M D d  
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G un & S In N w Y k N Y 1958 P \$6 75
- A SKEPTICAL PSYCHOANALYST by K th M k C l by M D 145 p g  
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M S M d 134 p g ll t t d Ch l C Th m P b-  
l h Sp gf ld ill 1958 P \$8 50
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P \$10 50
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R k ff M D d Ab h m C t w M D 941 p g ll tr d  
P l B Hoeb In N w Y k N Y 1958 P \$18
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S Ep t M D 352 p g ll tr d L & Feb g Ph l d lph  
P 1958 P \$15
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197 p g ll tr t d Ch l C Th m P bl h Sp gf ld ill  
1958 P \$6 50
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P bl h Sp gf ld ill 1958 P \$12 50
- MEDICINE AND THE NAVY 1200-1900 by J J K l D S O R N  
V lum II 1649-1714 332 p g ll tr t d E & S L ing to Ltd  
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& W lk C mp y B l m Md 1958 P \$8 50





# UNITED STATES ARMED FORCES MEDICAL JOURNAL

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UNITED STATES  
GOVERNMENT PRINTING OFFICE  
WASHINGTON 1958



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# Monthly Message

## MILITARY ASSISTANCE ADVISORY GROUPS (MAAG)

On a recent visit to Turkey it was our privilege to observe the development of our military assistance along medical lines. Lt Colonel Samuel B Caldwell MC USA has been attached to the group in Ankara for the past two years. The Turkish Medical Field Service School was established at Izmir under his guidance. I visited this school two years ago and again in April 1958 with Dr B N Carter and Brigadier General S S Brownton USAF (MC).

The school is under the command of a general officer of the infantry with medical advisors and consists of two parts one for the enlisted men and one for the officers. The initial period of training is basic infantry drill and the school of the soldier. In the medical sections two hospitals have been established with United States equipment a MASH unit and a field hospital. In an adjacent area officers quarters are being built and nearby is a school of aviation.

The hospital units have been so well trained that earlier in the year they moved to a town in the south of Turkey which had been completely destroyed by an earthquake and operated with great efficiency. At the time of our visit they were re-established and fully manned appeared exactly as do our own units and were functioning in exactly the same fashion. Both the officers and noncommissioned group were justly proud of their units and of their training systems.

While there luncheon was being prepared and we found it extremely well cooked varied and most palatable. Since beginning this training program 18 000 officers and men have been trained and are completely familiar with the program and their field units. Such training has far reaching effects because as the personnel return to their homes after their periods of service they carry their knowledge with them and contribute to the whole medical economy of Turkey.

*Frank B Berry*

FRANK B BERRY M D  
Assistant Secretary of Defense  
(He 1th and 1 dic 1)

# UNITED STATES ARMED FORCES MEDICAL JOURNAL

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Volume IX

November 1958

Number 11

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## THE TREATMENT OF ACUTE APPENDICITIS UNDER SUBOPTIMAL CONDITIONS

TANNER F. BOTERS *Colonel, MC, USA*  
C. L. L. & HUGHES *Lieutenant Colonel, MC, USA*  
KENNETH B. BOJILL *Captain, MC, USA*

FOR the past generation it has been taught that acute appendicitis is a surgical emergency and that "the sun must never set" on a case of appendicitis without operation. Certainly there must be circumstances where appendectomy should be deferred and the patient transferred urgently because of unavailability of a physician or surgeon. Lack of surgical training of the physician, a signed lack of facilities for safe anesthesia, lack of suitable mechanical equipment or for other reasons not inherent in the patient or his disease. Possibly surgeons have oversold the concept that appendectomy can be accomplished as an emergency at all costs and it may be that we now should stress the matter of judgment as to when, where and under what circumstances appendectomy should be undertaken. Remote military installations are especially likely to be suboptimally prepared to cope with major operative surgical procedures and a hospital such as ours is especially apt to see the results of such problems where solution has been attempted under something less than the most favorable circumstances.

Trainer Army Hospital serves not only as a general hospital for the care of duty personnel of the armed services and their dependents but also serves patients entitled to medical care through the U. S. Coast Guard, Merchant Marine, U. S. Public Health Service, Veterans Administration, Civil Service and the various foreign consular services. The area served covers a wide area including many remote military installations and ships.

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From Trainer U. S. Army Hospital, APO 413 San Francisco, Calif.

at ea The general surgery service of this hospital recently received a series of patients with acute appendicitis originally seen and treated at one or more of these installations. Operative treatment had been attempted in one group of cases with unfavorable results. In the other group of equal size conservative measures of parenteral antibiotic therapy, bed rest and relief of pain had been used with much less morbidity and fewer complications. It is not the purpose of this paper to criticize treatment given elsewhere and every sympathy surely is with the physician or corpsman assigned where there are factors limiting the treatment given. However, the comparison between the two case groups is so striking that proper attention to duty requires that they be reported with suitable discussion.

### PATHOPHYSIOLOGIC BASIS FOR TREATMENT

Acute appendicitis is secondary to obstruction to the appendiceal lumen and inasmuch as the appendix is a secreting organ, the obstructed appendix is a closed loop subject to the phenomenon of tension gangrene. The lumen of the normal appendix is little more than a potential space containing 0.2 ml volume. The appendix secretes at the rate of 2 ml per 24 hours with a slight early increase in rate for the obstructed organ. Experimental evidence shows that the human appendix will rupture when distended by 5 ml of fluid. Correlation of these bits of information indicates in general that the obstructed appendix will tend to rupture in 48 hours unless the obstruction is overcome by the intraluminal pressure or appendectomy stops the chain of event.

There are several variable factors which make prediction hazardous. For example, there is no way to tell whether or not the obstruction is absolute or whether it can be overcome readily by pressure. Further, there is no way to know the exact duration of the disease process because we depend on the patient's complaint of pain which is based on his individual threshold. Fortunately, there are other facts which help us. Perforation takes place distal to the point of obstruction and, as has been shown, at perforation about 5 ml of material will be spilled into the peritoneal cavity. The lumen tends to remain obstructed so that there are no successive increments of peritoneal contamination in the usual case. Instead, there is the one 5 ml soiling. This explains why localized peritonitis or abscess formation is seen rather than generalized peritonitis which is infrequent. These facts indicate that we have about 48 hours before perforation and soiling is apt to be minimal. It has been fairly generally accepted that appendectomy is a prophylactic procedure to prevent perforation, but if perforation already has occurred, appendectomy may be delayed until after the localized peritonitis has subsided. That this is the usual train of events is well documented.

With the advent of sulfonamides and later, penicillin and streptomycin, the mortality and morbidity from complications of appendicitis were reduced markedly. As early as 1940, Ravdin, Rhoads, and Lockwood<sup>3</sup> reported excellent results from use of sulfonamides in treatment of appendical peritonitis. In 1945, Ochsner and Johnston<sup>4</sup> reported the use of sulfonamides for localized appendical peritonitis, reserving operation for cases where peritonitis tended to become generalized. They reported that with nasogastric suction, sulfonamides, blood transfusions, and plasma, 75 to 80 per cent of instances of localized appendical peritonitis resolved without surgical drainage. In 1946 Crile<sup>5</sup> reported 50 cases of appendicitis with peritonitis treated with large doses of penicillin with no instance where a subsequent abscess required surgical drainage. Most of these patients were afebrile and taking oral feedings within 72 hours. Pulaski, Artz, and Baker reported uniformly excellent results in localized and spreading appendical peritonitis using Terramycin (brand of oxytetracycline). From these papers, and others, it is clear that appendical peritonitis usually is not attended by great risk to life if treated by sulfonamides and/or antibiotics. However, to speak against appendectomy was and is medical heresy so that few reports of deliberate omission of operation in early acute appendicitis are seen. Harrison<sup>7</sup> made one such report, documenting 47 cases of early acute appendicitis treated by antibiotics in 1953. The average duration of illness prior to treatment was 18 hours and treatment consisted of bed rest, nothing by mouth, morphine for relief of pain and penicillin on the Crile plan of 100,000 units every two hours intravenously for the first 48 hours. Two patients progressed to appendical perforation and abdominal mass formation. Fourteen had peritonitis from appendical perforation when seen, most responding to penicillin alone but a few requiring in addition Terramycin intravenously in doses of 500 mg every 12 hours. Nasogastric suction was not used routinely in this series.

Jordan and Hallenbeck, in reporting the current trends in the treatment of appendicitis at the Mayo Clinic, outlined the ideal method of conservative treatment for early peritonitis associated with acute appendicitis, suggesting that general support of the patient should include oxygen as necessary, warm packs to the abdominal wall and opiates for relief of pain. The patient's fluid and electrolyte needs should be maintained with intravenous replacement therapy and with blood or plasma as indicated. Gastrointestinal distention should be relieved by decompression and Wangensteen suction. The inflammatory reaction in the peritoneum should be controlled with large doses of penicillin and streptomycin sulfate or with intravenous tetracycline hydrochloride. The recommended dosage of penicillin was 600,000 units every 12 hours with one-half gram dihydrostreptomycin every six hours. The dosage of tetracycline

hydrochloride was given as 500 mg intravenously every six hours

### MATERIAL

Over a nine month period beginning 1 Jul 1954 14 patients with acute appendicitis were transferred to this hospital after receiving initial therapy in a remote or isolated installation where facilities for appendectomy were inadequate from the standpoint of assigned personnel or available equipment Group A consisted of seven patients in whom appendectomy was performed or attempted before transfer and Group B consisted of seven patients in whom conservative regimen was employed initially with early evacuation to this hospital

### CASE REPORTS

#### Group A Appendectomy Attempted or Performed Before Transfer

**Case 1** This 19 year old young man transferred to this hospital some 30 hours following performance of an appendectomy in a isolated installation History related 11 hours prior to the operation consisting of typical generalized abdominal pain and vomiting with shifting of pain and tenderness to the right lower quadrant The appendectomy had been attempted through a low periumbilical incision and at the time of operation ulceration of the appendix was difficult Further difficulty was encountered with anthesis Originally a 1% solution of Procaine (brand of tetracaine hydrochloride) anesthetic had been attempted but this had to be supplemented by open ether The total time of the operation was listed as five hours Post operation the patient was found with fecal contamination present throughout the abdomen The treatment of the appendiceal stump was not known Closure of the peritoneal cavity and muscle layers had been complicated with interrupted silk sutures A No 14 ft rubber catheter had been placed through the primary incision into the peritoneal cavity for drainage Penicillin and streptomycin were administered parenterally

On admission to the hospital the patient showed a marked distended abdomen lack of peristalsis and a temperature of 99.4 F The wound was demarcated, reddened and drained Routine laboratory findings leukocyte count 11,000 with normal differential count The patient was continued on penicillin and streptomycin intravenously particularly with fluid supplements intravenously and gastrointestinal decompression On the second day of hospitalization the wound was packed because of serous drainage Suture removed and the wound was found to be grossly infected with quaternary iodine and subsequent closure by secondary intention The patient continued in the hospital was prolonged by large fluid intake and dynamic ileus for four days This patient total hospital stay was 24 days after which time he was discharged to light duty status

**Comment** A five hour operation for appendicitis is *prima facie* evidence that conservative management would have been safer and less traumatic. The use of silk sutures for wound closure in case of a ruptured appendix invites wound infection persisting until all sutures are extruded. Here, the sutures were removed, the wound was left open, and secondary closure was used after a clean wound had been attained. This patient may yet in the next several months return with drainage. Rarely should a drain be left in the peritoneal cavity itself, suction to remove free exudate being sufficient. If drainage is employed, a soft Penrose type drain rather than a catheter is better because a rubber tube may cause bowel erosion and fistula formation. A drain in the soft tissues of the abdominal wall is preferable to a drain in the peritoneal cavity because the wall is more vulnerable than the peritoneum whose prime function is to deal with organ

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**Case 2** This 21 year old man entered this hospital after a three day illness of generalized abdominal pain, nausea and vomiting, and later localization of pain to the right lower quadrant. An appendectomy had been planned with open-drop ether anesthesia. During the induction period the patient had developed severe laryngeal spasm and vomiting with resulting aspiration. Because of this the operation had been discontinued and 12 hours later under Pontocaine subarachnoid anesthesia a right sided McBurney's incision had been made through which the appendix had been visualized and found to be indurated and densely adherent to the surrounding structures. It was reported as having been neither suppurative nor gangrenous and the operating surgeon had decided not to remove the appendix. The abdominal cavity therefore had been closed. The patient then was transferred to this hospital.

On admission here his temperature was 101.2 F and he was in acute distress. Both lung fields revealed evidence of pneumonitis and atelectasis. The abdominal wound was indurated and tense. No bowel sounds could be heard. A leukocytosis was present. Roentgenograms of the chest substantiated the diagnosis of pneumonitis and bilateral lower lobe atelectasis. The patient was treated with large doses of penicillin and streptomycin sulfate administered intravenously, gastrointestinal decompression and intravenous fluids and electrolytes. On the second day of admission several sutures were removed from the wound followed by the release of considerable blood and sero-purulent material. The wound infection was treated with daily care and the wound was allowed to close secondarily. Approximately three weeks following admission an elective appendectomy was performed, the retrocecal appendix showing evidence of a recent acute inflammatory process. There were dense adhesions to surrounding structures and the peritoneum was thickened and friable. The pathologic report was that of subsiding acute appendicitis and gangrene. The total course in the hospital was 43 days.

Comment Vomiting and aspiration can happen in the best hands but had subarachnoid anesthesia been the original choice the pulmonary complications might have been avoided. Open drop ether is not necessarily the simple choice in an adult male patient and in the hands of an inexperienced anesthetist. There seems little to commend the philosophy of inspection of the appendix with the decision to leave it *in situ* because it does not look too bad. Even prophylactic appendectomy in a case of mistaken diagnosis is preferable.

**Case 3.** This 28-year-old man entered this hospital two months following the initial illness consisting of abdominal pain which had developed in an isolated stricture. He had been treated initially with mineral oil and castor oil. About six days following the onset of illness the patient had had a transient colic pain with the abdomen with accompanying fever and distention. He had been transferred to a larger institution where an exploratory laparotomy was performed with the preoperative diagnosis of acute appendicitis. At the time of surgical intervention a large amount of free purulent material had been found in the abdominal cavity. Removal of the appendix had not been attempted. A large abscess cavity beneath the rectum had been drained and the abdominal cavity had been closed. Postoperatively the patient had had periods of diarrhea and recurrent temperature elevation and a subquadrant mass had developed in the left lower quadrant of the abdomen. A second exploratory operation was performed and a large amount of purulent material was drained from the left lower quadrant mass. The patient again developed fever and pain and a third time the middle of the lower abdomen was found which required incision and drainage. The patient was treated with multiple antibiotics during the initial hospitalization and then was transferred to this hospital for further care.

On examination at this hospital the patient appeared clinically ill and debilitated. His oral temperature was 100.8 F. His pulse and blood pressure were normal. Examination of the abdomen revealed severe tenderness with two draining sinuses extending into the left lower quadrant of the abdomen both of which could be palpated down through the abdominal musculature. There was generalized tenderness in the entire abdomen but no masses could be felt. Sinus tract injections with Lipiodol (brand of contrast medium) revealed that the tracts to be multiple throughout the anterior abdominal wall. A barium enema revealed no connection between the large bowel and the abdominal sinuses. Shortly after admission a fecal material was voided a distance from the sinus tract. These were treated with local irrigations and later a continuous sinus catheter. Approximately 100 ml of purulent foul mellow material was discharged daily. Drainage ceased with two weeks and a planned laparotomy revealed perforated appendix lying to the middle segment of the cecum. The appendix was removed with undisturbed the abdominal cavity was closed. On the eighth postoperative day the patient died of an inflammatory mass in the old iliac fossa in which was drained of approximately 400 ml of pus. The wound was treated by saline

irrigations and allowed to heal by secondary intention. The remainder of the patient's stay in the hospital was complicated by recurrence of purulent discharge from the two sinus tracts in the left lower abdomen which subsequently closed. The patient's total time away from duty was approximately 240 days at which time he was discharged to a light duty status.

**Case 4** This 32-year-old man entered the hospital after a three-day history of abdominal pain with localization in the right lower quadrant. He had been operated on the second day of his illness at a remote installation. The surgeon had made a right lower quadrant McBurney's incision which later had been extended vertically for added exposure. The appendix lay high in a retrocecal position being grossly gangrenous throughout its length. The operative procedure had lasted six and one-half hours. No drains had been placed in the wound and the patient had been started on penicillin and streptomycin sulfate postoperatively.

On admission to this hospital—on the first postoperative day—the patient was acutely ill. His oral temperature was 103.2°F, his pulse rate was 104 per minute, his abdomen was distended and he was vomiting. No abdominal masses could be felt. He was continued on intravenous penicillin and streptomycin sulfate and fluid and electrolyte as necessary for a 10-day period. On the seventh day a wound abscess became apparent and the sutures were removed. The wound was opened wide and treated with local irrigation and allowed to close by secondary intention. Following healing of the wound the patient was returned to a light duty status after 23 days of hospitalization.

**Comment** Inasmuch as this patient was transferred to this hospital on the day after operation, he might just as well have been transferred before operation, thus avoiding a six and one-half hour procedure. Major surgery should not be performed in an installation where appendectomy requires this length of time.

**Case 5** This 25-year-old man entered this hospital after having undergone an appendectomy at another installation two days prior to his admission here. The duration of illness had been some 40 hours prior to the surgical procedure. The appendix had been reported as gangrenous with a small perforation present.

On admission to this hospital the patient was comfortable and had a normal temperature and pulse. Bowel sounds were present and normal. The patient was treated in the usual manner with regular diet and ambulation about the ward. On the seventh postoperative day redness and induration became apparent about the wound which required removal of the sutures and drainage of a large wound abscess. This was irrigated and after 10 days was closed secondarily with stainless steel wire. Healing was rather slow and the patient was discharged to light duty after a total of 41 days lost from duty.

**Case 6** An appendectomy was performed on a 46-year-old white man who had developed symptoms and signs of acute appendicitis 72 hours



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Case 3 This 28 year-old male patient had this history for two months following the initial illness consisting of abdominal pain which had developed in an isolated installation. He had been treated initially with mineral oil and cecum. About six days following the onset of illness the patient had had intensification of pain within the abdomen with accompanying fever and distention. He had been transferred to a larger installation where an exploratory laparotomy was performed with the preoperative diagnosis of acute appendicitis. At the time of surgical intervention a large amount of free purulent material had been found in the abdominal cavity. Removal of the appendix had not been attempted. A large abscess cavity beneath the rectus sheath had been drained. The abdominal cavity had been closed. Postoperatively the patient had had periods of diarrhea and recurrent temperature elevations and a subsequent mass had developed in the left lower quadrant of the abdomen. A second exploratory peritoneotomy was performed and a large amount of purulent material was drained from the left lower quadrant mass. The patient again developed fever and pain and a third mass in the middle of the lower abdomen was found which required incision and drainage. The patient was treated with multiple antibiotics during the initial hospitalization and then was transferred to this hospital for further care.

On examination at this hospital the patient appeared chronically ill and debilitated. His oral temperature was 100.8 F. His pulse and blood pressure were normal. Examination of the abdomen revealed several scars with two draining sinuses in the left lower quadrant of the abdomen both of which could be probed down through the abdominal musculature. There was generalized tenderness in the entire abdomen but no masses could be felt. Six tracts injected with L. p. 0.1 (brand of contrast medium) revealed the tract to be multiple through the anterior abdominal wall. A barium meal revealed no connection between the large bowel and the abdominal sinus tract. Shortly after admission fecal material was noted to drain from the sinus tract. The tract was treated with local irrigations and later a continuous irrigation catheter. Approximately 100 ml of purulent foul smelling material was discharged daily. Drainage ceased within two weeks. A second exploratory laparotomy revealed a perforated appendix lying in the medial aspect of the cecum. The appendix was removed with difficulty through the abdominal incision. On the eighth postoperative day the patient developed a firm mass in the left lower quadrant in the incision which had a diameter of approximately 400 ml. The mass was treated by saline

operatively. He was transferred to this hospital on the second day following operation.

On admission to this hospital the patient's temperature was 101.4°F. General physical examination revealed a rather acutely ill patient with a quiet distended abdomen. There was erythema and tenseness about the right lower quadrant wound. Several silk sutures were removed to allow drainage of serous material. On the sixth postoperative day bile stained drainage was seen exuding from the wound. Following this a definite fecal fistula developed which was controlled with continuous catheter suction followed by intermittent saline irrigations and spontaneous closure of the fistula after 21 days. The patient's total hospital stay was 29 days following which he was returned to a light duty status for further convalescence.

**Comment** Fecal fistula occurs infrequently after appendectomy and there is no agreement as to whether the appendical stump should be inverted. Unfortunately in the cases where there is such severe reaction that stump ligation is insecure, there usually is such severe cecal reaction that placement of a purse string suture is hazardous so that when stump inversion is most needed it technically may not be feasible.

#### Group B Conservative Regimen Employed Before Transfer

**Case 1** This 19 year old youth entered this hospital after a four day history of generalized abdominal pain with localization in the right lower quadrant the onset of which occurred while he was on board a naval vessel. A corpsman on the vessel thought that the patient had acute appendicitis and had subsequently placed him on complete bed rest, nothing by mouth and intravenous administration of dextrose and water with penicillin and streptomycin added. The patient stated that within 36 hours he was relatively asymptomatic. He was first seen at this hospital four days after the onset of the illness.

The physical examination was entirely within normal limits with the exception of deep poorly localized tenderness in the right lower quadrant. Blood cell count, urinalysis and a roentgenogram of the chest were normal. The patient was continued on penicillin and streptomycin sulfate but he was ambulatory and was given a soft diet. On the tenth day of illness an elective appendectomy was performed. At the time of surgical intervention the appendix was retrocecal in position and showed definite signs of acute and chronic inflammatory changes with fresh adhesions to surrounding structures. No perforations were seen. The pathology report confirmed the diagnosis of acute suppurative appendicitis. Postoperatively the patient's course was essentially normal and he was discharged to a full duty status on the fourteenth day.

**Comment** In the absence of a doctor the enlisted corpsman showed excellent judgment which contributed to an uncomplicated course and excellent recovery. It is interesting that ten days after onset there was no perforation.





**Case 2** This 20-year-old youth developed generalized abdominal pain with localization in the right lower quadrant and nausea and vomiting while on board a naval vessel 10 days prior to admission to this hospital. He was started on penicillin and streptomycin sulfate in conjunction with intravenous fluid therapy, complete bed rest, and nothing by mouth. He stated that he was asymptomatic from the fifth day of illness. Physical examination was entirely within normal limits, as were his oral temperature and routine laboratory work. The patient was observed for two days without antibiotic therapy and remained afebrile and comfortable. On the following day the eleventh day following the onset of illness, an appendectomy was performed which revealed an inflamed appendix in a retrocecal position with fresh inflammation surrounding it but without perforation. Microscopic examination revealed both acute and chronic inflammatory changes. The patient's postoperative course was essentially uneventful and he was returned to a full duty status after 18 days.

**Case 3** This 21-year-old man entered this hospital after eight days of illness consistent with the impression of acute appendicitis. He had been treated on board a naval vessel with complete bed rest, a liquid diet, and large doses of penicillin for a four-day period, thereby beginning on the third day of illness.

Physical examination findings on admission to this hospital were entirely within normal limits. Tests were routine laboratory studies and a roentgenogram of his chest. The patient was continued on penicillin and streptomycin was added. He was given a regular diet and ambulatory privileges about the ward. After five days of observation, an elective appendectomy was performed. Findings at operation consisted of a absiding acute appendicitis which was confirmed by pathologic examination. The patient's postoperative course was complicated by furunculosis which lengthened his hospitalization to a total of 30 days. He then was returned to full duty.

**Case 4** This 20-year-old youth entered this hospital 36 hours after the onset of abdominal pain with associated nausea and vomiting, characteristic of acute appendicitis. Treatment instituted on board a naval vessel had consisted of complete bed rest, nothing by mouth, and large doses of penicillin. He was evacuated to this hospital by air.

On admission his oral temperature and pulse were normal. General physical examination revealed point tenderness with moderate spasm over the right lower quadrant of the abdomen with rebound tenderness. A mild leukocytosis was present. He underwent an appendectomy on the day of admission. The operative findings were those of acute purulent appendicitis. His postoperative course was uneventful and he was discharged to full duty status on the twentieth day.

**Case 5** This 21-year-old male was seen in this hospital five days after the onset of abdominal pain, nausea, and vomiting while he was on board a naval vessel. The diagnosis of acute appendicitis was

made and intravenously administered penicillin and streptomycin were started. Within 72 hours the patient was comfortable and asymptomatic. Routine laboratory studies and a roentgenogram of the chest were normal. Antibiotics were discontinued and the patient was observed for two days. He remained afebrile and comfortable. On the seventh day of illness an appendectomy was performed with the findings at operation being that of acute appendicitis with suppuration but without perforation present. The pathology report substantiated the above diagnosis. The patient's postoperative course was uneventful and he was returned to a duty status on the sixteenth hospital day.

**Case 6** This 13 year old boy entered the hospital on the second day of illness characteristic of acute appendicitis. Under spinal anesthesia an appendectomy had been attempted on board a naval vessel but because of an inadequate anesthetic level only a skin incision had been made. The patient had then been treated with penicillin, streptomycin sulfate and Terramycin intravenously and transferred to this hospital.

On admission to this hospital the patient had an oral temperature of 99.8 F and a pulse rate of 80 per minute. He had generalized abdominal tenderness with localization to the right lower quadrant. No masses were palpable. The skin incision had been sutured. He was continued on penicillin and streptomycin sulfate for five days after which an elective appendectomy was performed. At the time of surgery the appendix was mildly injected, contained a moderate sized fecalith and was loosely adherent to surrounding structures. Pathologic examination revealed a leukocytic infiltration to the appendiceal wall with the diagnosis of subsiding acute appendicitis and early gangrene. No perforation was found. The patient's postoperative course was uneventful and he was discharged on the fourteenth postoperative day.

**Comment** The doctor in this case is to be commended for his good judgment in desisting in operative attempts in the face of inadequate ancillary facilities. Persistence might have resulted in a complicated course.

**Case 7** This 18 year old white male had the onset of generalized abdominal pain with localization to the right lower quadrant 48 hours prior to admission to this hospital. He was treated initially with mineral oil and enemas with gradual intensification of pain with radiation to the right testicle and in the right shoulder. On physical examination his oral temperature was 99.8 F but the patient was rather acutely ill with diffuse abdominal tenderness present. No masses could be palpated. Admission white blood cell count was 18,900 per  $\mu$ l with a marked increase in neutrophils. Urinalysis and a roentgenogram of the chest were normal. At the time of admission it was believed that the patient had an early perforation of the appendix. At the time of operation a small perforation was found with contamination of the surrounding peritoneum. The appendix was removed and the wound was drained postoperatively. Penicillin and streptomycin sulfate were added to intravenous feedings. A wound abscess developed which

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Physical examination following admission to this hospital were entirely within normal limits as were routine laboratory studies and nothing remarkable of his chest. The patient was continued on penicillin and streptomycin was added. He was given a regular diet and ambulatory privileges but remained in the ward. After five days of observation an elective appendectomy was performed. Findings at operation consisted of subducing acute appendicitis which was confirmed by pathological examination. The patient's postoperative course was complicated by furunculosis which lengthened his hospitalization to a total of 30 days. He then was returned to full duty.

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# NONTOXIC THYROID NODULES

## A CLINICAL DILEMMA

LAWRENCE S GREENE L t t MC USNR

MUCH has been learned about thyroid physiology and pathology since the turn of the century. Certain pathways of iodine metabolism have been clarified and several distinct thyroid hormones have been isolated. The use of iodine 131 ( $I^{131}$ ) and serum protein bound iodine determinations have aided in the problem of diagnosis of thyroid disorders. Treatment of thyroid disease has also been facilitated largely due to the availability of radioactive iodine and anti-thyroid drugs as well as improvement in surgical technique.

Despite numerous advances much concerning nontoxic thyroid nodules remains unknown especially with regard to treatment. The importance of possessing a clear and distinct approach to such nodules cannot be underestimated because carcinoma of the thyroid gland frequently presents to the clinician in the form of such nodular lesions.

It is the purpose of this review to present current information which will help the practicing physician secure a rational approach to nontoxic thyroid nodules. Particular emphasis will be placed upon the multiple problems concerning the occurrence, detection and therapy of nodules representing thyroid carcinoma.

### EVOLUTION OF NODULAR GOITER

Nodular goiter is an entity of diverse etiologic factors the most important of these being iodine lack. The average adult requires 100 to 200 micrograms of iodine per day; this requirement is somewhat greater in childhood and adolescence. Many goitrogens also have been incriminated in the cause of nontoxic goiter. These include minerals such as calcium, fluorine and chloride; drugs such as thiocyanate, perchlorate, cobalt, resorcinol, para-aminosalicylic acid (PAS), sulfonamides; and certain foods particularly cabbage, rutabaga and soybeans. Taylor utilized radioautography in over 100 patients with various types of simple goiter. The five stages listed below present his reconstruction of the evolution of nodular goiter.

*Stage 1* Diffuse hyperplasia leading to a soft, vascular thyroid. Often the radioactive iodine uptake was increased. Histologically these glands possessed small follicles with moderate amounts of colloid.

*Stage 2* This stage consists of either of two situations:

a Multiple discrete areas of hyperfunction consisting of small follicles

b Solitary hyperactive nodules

*Stage 3* The foci of intense hyperactivity of the preceding stage appeared to inevitably progress to hemorrhage followed by central necrosis.

*Stage 4* More of the nodules progressed to the point of becoming inactive autoradiographically.

*Stage 5* The end result being multinodular nontoxic goiter occurring as a consequence of repeated hyperplasia and destruction within the gland.

### FREQUENCY OF CARCINOMA OF THE THYROID

The accurate incidence of carcinoma of the thyroid has created vigorous debate for many years. Opinion is sharply divided between those groups who believe that the disease is relatively common and those who maintain that it is a rare entity. Furthermore, there is even greater disagreement regarding the frequency of carcinoma in thyroid nodules of all types. Naturally, such conflicting opinions led to irreconcilable differences in judgment concerning therapy of these nodules.

Sokal<sup>2</sup> in an authoritative discussion of the incidence of thyroid carcinoma, reviewed 122,000 cases of carcinoma of all types. Included in his review was a series of cases reported by Dorn that represented 10 metropolitan areas of the United States, among which were goiter endemic areas. Dorn had enlisted the aid of every hospital and 98 per cent of the practicing physicians in these areas in order to obtain an accurate estimate of the total number of cases of cancer of all types under observation or treatment in these representative communities. Sokal concluded from his review of the literature that the average incidence of carcinoma of the thyroid was 0.56 per cent of all clinical carcinomas. He expressed the significance of the preceding figure as follows: "In a typical community of 1,000,000 people, there would be 25 patients with thyroid cancer."<sup>2</sup> Further emphasis on the infrequent occurrence of carcinoma of the thyroid is derived from the fact that this malignancy stands seventeenth in the list of cancers causing death and is only one thirty-seventh as common a cause of death in women as cancer of the breast.

Conversely, Alexander<sup>3</sup> studied the occurrence of thyroid cancer in San Francisco and showed the prevalence to be far in excess (by approximately 400 per cent) of the hypothetical

value laid down by Sokal. Similarly surgeons operating on the thyroid gland maintain with rare exception that the frequency of carcinoma of the thyroid is much greater than the figure reported by Sokal.

Table 1 gives statistics of the incidence of carcinoma in thyroid surgical specimens from representative clinics throughout the country.

Source	Clinic	City	Year	No. of	No.
1. Connors	Lah.	San Francisco	1948	78	53
2. Hoen	San Francisco	San Francisco	1948	79	3
3. Rubenbord	San Francisco	San Francisco	1948	79	3
4. Aron	San Francisco	San Francisco	1948	79	3
5. Aron	San Francisco	San Francisco	1948	79	3
6. Aron	San Francisco	San Francisco	1948	79	3
7. Aron	San Francisco	San Francisco	1948	79	3
8. Aron	San Francisco	San Francisco	1948	79	3
9. Aron	San Francisco	San Francisco	1948	79	3
10. Aron	San Francisco	San Francisco	1948	79	3
11. Aron	San Francisco	San Francisco	1948	79	3
12. Aron	San Francisco	San Francisco	1948	79	3
13. Aron	San Francisco	San Francisco	1948	79	3
14. Aron	San Francisco	San Francisco	1948	79	3
15. Aron	San Francisco	San Francisco	1948	79	3
16. Aron	San Francisco	San Francisco	1948	79	3
17. Aron	San Francisco	San Francisco	1948	79	3
18. Aron	San Francisco	San Francisco	1948	79	3
19. Aron	San Francisco	San Francisco	1948	79	3
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74. Aron	San Francisco	San Francisco	1948	79	3
75. Aron	San Francisco	San Francisco	1948	79	3
76. Aron	San Francisco	San Francisco	1948	79	3
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96. Aron	San Francisco	San Francisco	1948	79	3
97. Aron	San Francisco	San Francisco	1948	79	3
98. Aron	San Francisco	San Francisco	1948	79	3
99. Aron	San Francisco	San Francisco	1948	79	3
100. Aron	San Francisco	San Francisco	1948	79	3

## OCCURRENCE OF CARCINOMA IN THYROID NODULES

Disagreement concerning the incidence of thyroid carcinoma per se is intensified with regard to its occurrence in and relation to nodules. Table 2 illustrates the frequency of carcinoma found in thyroid nodules of various types. There is some agreement that solitary thyroid nodules are more often the site of malignancy than multinodular glands.

Source	Clinic	City	No. of	No.
1. Aron	San Francisco	San Francisco	79	3
2. Aron	San Francisco	San Francisco	79	3
3. Aron	San Francisco	San Francisco	79	3
4. Aron	San Francisco	San Francisco	79	3
5. Aron	San Francisco	San Francisco	79	3
6. Aron	San Francisco	San Francisco	79	3
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11. Aron	San Francisco	San Francisco	79	3
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34. Aron	San Francisco	San Francisco	79	3
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64. Aron	San Francisco	San Francisco	79	3
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95. Aron	San Francisco	San Francisco	79	3
96. Aron	San Francisco	San Francisco	79	3
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98. Aron	San Francisco	San Francisco	79	3
99. Aron	San Francisco	San Francisco	79	3
100. Aron	San Francisco	San Francisco	79	3

There are several reasons why statistics derived from surgical thyroid specimens may be misleading. Such figures are necessarily obtained from a carefully selected population. Crile and Dempsey pointed out that these patients are carefully screened first by the patient himself who does not often consult a doctor until the nodule is giving evidence of growth or function.

The natural history of thyroid carcinoma, especially the papillary variety, is often very long<sup>11</sup> with no alteration in growth for periods as long as 10 to 20 years.

Clinical differentiation of solitary nodules from multiple nodules is notoriously difficult, as clearly illustrated by infrequent pathologic and clinical agreement.

Furthermore, the accuracy of differentiating benign from malignant thyroid lesions remains subject to much disagreement. Using histologic evidence of blood vessel, lymphatic, or capsular invasion, and invasion of normal adjacent gland as criteria has not eliminated this confusion. Histologic criteria also have been found to be notoriously inaccurate in determining the prognosis of this malignancy.

### PREOPERATIVE DIFFERENTIATION

The use of radioactive iodine has been extended from diagnosis and therapy of thyroid disorders to the investigation of characteristics that supposedly differentiate benign and malignant thyroid nodules. Rawson and his collaborators,<sup>12</sup> and Dobyns and Maloof<sup>13</sup> found that the maximum uptake of any of the cancerous nodules was decidedly less than that of normal adjacent thyroid tissue. In 1950, Evans<sup>14</sup> stated: "So far we have never found a hot nodule which has shown histologic evidence of malignancy."

Using special isotopic technic, Perlmutter, Slater, and Attie<sup>1</sup> compared the relative avidity for  $I^{131}$  of clinically solitary nodules or nodules limited to one lobe with that of the contralateral uninvolved part of the gland. A nodule was classified as "hot" if it collected considerably more radioisotope than the contralateral side, and as "cold" if it collected considerably less than the other side. Those with intermediate values were considered to be "warm" nodules. In 1954 these authors reported a study of 83 such clinically solitary nodules. None of the 24 "hot" nodules were found to be malignant but 20 per cent of the warm and 72 per cent of the cold nodules were classified as malignant by the surgical pathologist. Since this original study their series of cases has been extended to 140, the findings remaining the same. Johnson and Beierwaltes<sup>15</sup> carried out a similar study with results comparable to those of Perlmutter, Slater, and Attie. Since the beginning of this use of  $I^{131}$ , clinically solitary "warm" and "cold" nodules have been grouped separately from "hot" solitary nodules regarding the suspicion of carcinoma, with the former two types considered highly suspicious as to malignancy. The definition of a "hot" nodule is considered by these authors<sup>16</sup> to be one which concentrates at least 125 per cent as much  $I^{131}$  as the non nodular portion of the gland. A nodule that concentrates less than 125 per cent  $I^{131}$  compared to the remainder of the gland is considered "cold." Perlmutter and Slater<sup>17</sup> also used  $I^{131}$  with directional counting,

over multinodular glands with predominant nodules for a similar purpose. However, it must be stressed that the distinction between hot and cold nodules applies only to clinically solitary nodules. Sufficient study of multinodular goiters using this technic has not been done as yet.

### CHOICE OF THERAPY

The controversy with regard to nodular thyroid disease quite understandably extends to the various aspects of therapy for this condition. Hinton and Lord offered a simple solution to the entire problem stating that all nontoxic thyroid nodules be removed regardless of whether they appear clinically to be solitary or multiple. Their reason for this opinion was their belief that a large number of such nodules will contain unsuspected carcinoma. Cerise, Randall and Ochsner concurred in this policy of removal of all thyroid nodules. This approach was defended by virtue of their opinion that one is unable to differentiate carcinoma from benign nodular goiter in 50 per cent of all cases. Removal of all thyroid nodules is advocated by other surgeons.

Hermanson, Gargill and Lesses reiterated the opinion that all thyroid nodules should be removed regardless of the clinical suspicion separating solitary from multinodular lesions. They defended this policy by repeating the well known dictum that the clinical differentiation of solitary from multiple nontoxic nodules is notoriously inaccurate. More important they stated that asymptomatic multinodular goiters should be considered as potentially malignant.

Those who believe that surgery is the treatment of choice in all nodules justify this policy by one or more of the following generalizations: (1) Cancer of the thyroid is fatal. (2) The person in whom cancer is found unexpectedly has a much greater chance of survival than one in whom the disease is clinically suspected. (3) Removal of all nodular goiters eliminates potential carcinoma.

Sloan offered a more conservative approach and suggested that all clinically discrete thyroid adenomas should be removed especially in young people and male patients. Adherents to this philosophy state that all nontoxic goiters should not be removed unless clinical suspicion of carcinoma is present such as fixation of a nodule, lateral cervical or Delphian node metastasis, hoarseness, dysphagia or other local symptoms and signs are present.

In 1954, Sokal might be expected from earlier expressions of his opinion urged that the great majority of nontoxic nodular goiters need not be extirpated. It was his opinion that enlargement of discrete tumors of the thyroid and nodule producing direct pressure symptoms warrant removal. On the other hand

soft, smooth, round nodules that do not grow may be treated with iodine or desiccated thyroid extract in order to observe the effect of these medications on the size of the nodules, or they may be left alone. He believed that it is justifiable to observe all nodules for a reasonable period.

The rationale for the use of thyroid in the therapy of nodular disease of this gland dates back as far as 1894. In 1917, Greer and Astwood<sup>2</sup> reported excellent results using desiccated thyroid in the treatment of patients with single or multiple nontoxic nodules. Regression in the size of the lesions occurred in a considerable number so treated. Greer and Astwood implied that a reduction in the nodule size, presumably brought about by thyroid stimulating hormone (TSH) suppression with thyroid extract, is an indication that nodule formation represents a physiologic rather than a pathologic process.

Crile<sup>12</sup> reiterated the views held by Greer and Astwood and stated that nontoxic nodular goiter arises because of primary failure of thyroid epithelium to secrete sufficient thyroid hormone. There is resultant stimulation of pituitary TSH production, with compensatory thyroid enlargement.<sup>25</sup> He pointed out the futility of subtotal thyroidectomy in the treatment of thyroid disease, because this aggravates the decompensation and further stimulates the production of TSH, causing hyperplasia and further nodule formation in the thyroid remnant. The high incidence of recurrent nontoxic nodular goiter in addition to the discovery of carcinoma in thyroid remnants, is explained in this manner. There is clinical confirmation to support the opinion that thyroid cancer may be stimulated to rapid growth by excess pituitary TSH. Conversely, such have been shown to regress when thyroid extract is employed, which diminishes TSH output. Hence, Crile stated that thyroid extract is the treatment of choice for small nodular goiters, but that large nodular glands should be removed if excessive pressure or neck disfigurement arises. Removal of all multinodular goiters is not advocated because of the frightening morbidity and mortality associated with total thyroidectomy, an operation which must be utilized if one believes all thyroid nodules represent or will become cancer.<sup>26</sup>

With respect to clinically solitary adenomas occurring in youth, Crile advocated removal of all these because they frequently represent papillary carcinomas or adenomas that behave like malignant lesions. Between the ages of 40 to 60 years, despite the frequency of involutional nodules in thyroids of this age group, papillary carcinomas and low grade nonpapillary carcinomas are common. Therefore, "all clinically discrete firm solitary tumors in middle age patients should be removed."

In patients over 60, nodules have often been present for many years and some of these may be calcified. The author

frequently benign and if malignant often grow so slowly that they rarely cause difficulty during the normal life expectancy of such individuals. Hence Crile reserved operative procedure for older patients when firm consistency of the nodules or history of recent growth arouses suspicion of existing carcinoma.

Miller further condemned the removal of all nodular thyroid glands. He defended his position by stating: "If the policy of removing all nodular thyroid glands was followed in this clinic it would be necessary to operate on 3 of every 100 new patients registered. The value of such an approach to the cure of thyroid cancer would be measured in maximum terms of one death a year if all such cancers arose in nodular goiters. The disadvantages in terms of morbidity, rare mortality, patient resistance, and increase in general cost of medical care seem to be prohibitive."

An attempt at a physiologic approach to solitary nodules was promulgated by Perlmutter and Slater. They recommended surgical removal of the goiter regardless of the results of laboratory investigation in patients under 25 years of age and in those with clinical evidence of neoplasia such as local lymph node enlargement, nodule fixation or hoarseness associated with vocal cord paralysis. In the remaining patients 24 hour I uptake, serum protein bound iodine (PBI) determinations and at times basal metabolic rates are performed. Determination of hot versus cold nodularity is routinely attempted by utilizing special isotope technic in clinically uninodular glands and in multinodular glands with predominant nodules. Surgical excision is advised in patients with normal total gland I uptakes possessing either cold or warm nodules and in patients with high total gland I uptake but possessing cold nodules. Hot nodules not responding to triiodothyronine therapy by reduction in size also are excised.

Finally Hurxthal and Heineman considered the following points: either lead to a clinical diagnosis of cancer or a high degree of suspicion of cancer or are indications for surgery.

All cases of clinical chronic thyroiditis without a clear history of acute thyroiditis in the past—this means a hard often diffusely involved thyroid gland.

Fairly recent or progressive enlargement of previously existing nodule or nodular goiter or both.

All firm or hard discrete nodules especially in patients under 50 years of age and children.

Firm persistent lymph node or nodules in the neck adjacent to the thyroid gland.

Nodular goiter discrete nodules due to surronding tissues.

Nodular goiter with laryngeal paralysis or neck pain without other adequate explanation or both

Toxic nodular goiters (Clinically toxic goiter is unlikely in a small solitary nodule)

All large nodular goiters causing considerable tracheal compression or unsightliness if the age and cardiovascular status of the patient justify operation<sup>27</sup>

### SUMMARY

Carcinoma of the thyroid is an uncommon lesion, probably representing less than 1 per cent of all cancer in an unselected population. It probably does not develop from a benign adenoma but originates as carcinoma per se. It occurs more frequently in clinically solitary nodules than in clinically multinodular glands.

Total thyroidectomy is probably the treatment of choice when surgical intervention is indicated, the clearest indications being in young people with clinically solitary nodules, in older people with "warm" or "cold" single nodules, or in any patient in whom a nodular thyroid is associated with local lymph node enlargement, tracheal compression, fixation to surrounding structures, or recent increase in nodule size that does not respond to therapy with thyroid extract. Whether or not multinodular thyroids deserve a surgical approach, unless there is clinical evidence of malignancy, is a highly debatable question.

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Finally the rapid enlargement of previously existing nodules and large toxic goiters.

All firm hard discrete nodules especially in patients under 50 years of age and in children.

Firm persistent lymph nodes on nodules in the neck adjacent to the thyroid gland.

Nodules of the thyroid gland due to surrounding tissues.



admission studies included a white blood cell count and differential hemoglobin determination urinalysis and roentgenogram of the chest. These and other laboratory studies were repeated when clinically indicated. Throat washings and paired serum specimens were obtained on all patients at the onset of the epidemic but these were discontinued when it was established that we were dealing with an epidemic of A/Japan/305/57 virus. Agglutination studies however were performed on several desperately ill patients late in the course of the epidemic and these also substantiated the clinical diagnosis of Asian influenza.

TABLE 1 Hospital admission of patients with influenza

Week of admission	Number of admissions	Patients		All patients	
		Number	Percentage	Number	Percentage
1	1	0	0	0	0
2	8	1	12.5	1	12.5
3	20	3	15.0	5	25.0
4	110	3	2.7	3	2.7
5	229	8	3.5	10	4.4
6	407	10	2.5	12	2.9
7	248	11	4.4	18	7.2
8	100	10	10.0	15	15.0
9	70	4	5.7	5	7.3
10	23	3	13.0	5	21.8
11	17	0	0	1	5.9
12	16	1	6.2	2	12.5
13	9	0	0	0	0
14	1	0	0	0	0
15	0	0	0	0	0
16	0	0	0	0	0
17	1	0	0	0	0
18	1	0	0	0	0
19	3	0	0	0	0
Total	1264	54	4.3	77	6.1

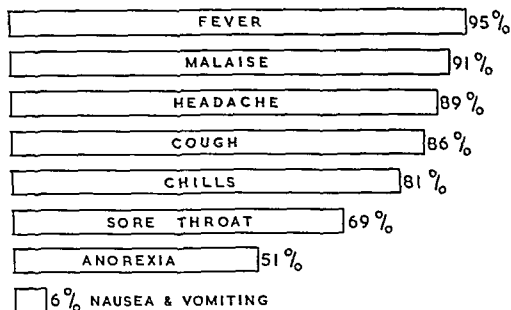
Routine treatment of the patients consisted of isolation from the general hospital population, bed rest, salicylates, high fluid intake, neo-synephrine nose drops (brand of phenylephrine hydrochloride) and a cough mixture (elixir of terpin hydrate with codeine). Antibiotics were not given unless indicated by the development of specific complications. Patients were not discharged from the hospital until they had been afebrile for at least 72 hours and had clinically recovered from the disease.

#### CLINICAL FEATURES

The most common symptoms (fig. 1) at the time of admission in the 119 adult patients were

1 *Fever* (95 per cent) Patients who did not have fever at the time of admission either gave a history of fever or developed a febrile reaction shortly after admission

2 *Malaise and myalgias* (91 per cent) The malaise varied from mild tiredness to severe prostration. The myalgias varied from generalized aching to low back pain, the latter being present in the majority of all patients



% 10 20 30 40 50 60 70 80 90 100

Figure 1 Frequency of specific symptoms in 1,264 cases of Asian influenza.

3 *Headache* (89 per cent) Most patients complained either of a dull, generalized frontal pain or of retrobulbar pain. The latter type was the most common. Very few patients required narcotics, and the headache disappeared after the first or second day.

4 *Cough* (86 per cent) During the first few weeks of the epidemic the cough was dry, irritative, and nonproductive; however, as the epidemic progressed, an occasional case with productive type of cough was noted.

5 *Chills* (81 per cent) The type varied from severe shaking chills to chilly sensations, the latter being more frequent.

6 *Sore throat* (69 per cent) The severity varied from a scratchy sensation to actual difficulty in swallowing.

7 *Anorexia* (51 per cent) In a few patients this was one of the major presenting complaints. It was interesting to note that this complaint was more common in women than in men (72 per cent as compared to 49 per cent).



effort was then instituted to discover the cause. A large number of the patients were found to have clinically asymptomatic respiratory complications of various types. Greene and Hair<sup>2</sup> reported the development of complications only in patients who failed to become afebrile within 72 hours. Only a minority of our patients who developed complications had the type of temperature curve described in their article.

After the pyrexia had subsided a large number of patients complained of severe sore throat but had no significant findings. This presented a problem in symptomatic therapeutics that gave no rewarding returns. In a few patients persistent hoarseness and hiccoughs became annoying and were resistant to any type of therapy.

In general, the complete physical examination of all patients upon admission revealed no abnormal findings except a non-specific pharyngeal infection in 75 per cent of the cases. A small percentage of patients showed enlarged cervical and axillary lymph nodes and febrile conjunctival infection. On rare occasions rhonchi, wheezes, and discrete rales were heard in the chest in spite of negative roentgenographic findings.

The hemogram was usually normal although 165 patients (14 per cent) showed an increase in the white blood cell count (above 10,000). A relative or absolute lymphocytosis was noted in approximately 4 per cent of patients.

As mentioned previously, routine chest films were obtained on all patients at the time of admission. In a number of the patients without complications there was a definite increase in the extent and prominence of the peribronchial markings. This is in keeping with the findings of Podosin and Felton.<sup>3</sup> In many instances it was possible to compare these admission roentgenograms either with previous or follow up roentgenograms. In this way the difference in the extent of these peribronchial markings was well demonstrated; however in the majority of cases this change was not present. These findings were not subjected to statistical analysis because the changes are relative and are often dependent on radiographic technique and interpretation and individual variation.

In pediatric cases the picture was not significantly different except that the children usually appeared more ill at the time of admission but responded more rapidly to treatment. In general, they seemed to tolerate their illness slightly better than the adults.

#### COMPLICATIONS

Although uncomplicated influenza is a mild disease with a low mortality rate the development of complicating illnesses markedly increases the dangers. The incidence of specific



The extremely high frequency of pneumonia in adult females (14 cases, 15 per cent incidence) was surprising. Even more striking was the finding that 10 of these 14 cases occurred in pregnant women. A total of 20 pregnant women were admitted to the hospital, giving a 50 per cent incidence of pneumonia in the gravid female with Asian influenza. Of the 10 gravid women, 8 were in the last trimester. There was pre-existing heart disease (mitral stenosis) of moderate severity in one of these patients. The only death in the series occurred in a patient with a term gestation who developed a fulminating pneumonia, myocarditis, and congestive heart failure three days before a normal delivery. Although temporary improvement was manifest shortly after delivery, the patient died suddenly on the third post partum day. Congestive heart failure developed in only 3 of the 54 patients with pneumonia. In each instance it occurred in gravid females in the third trimester and in each case was associated with a severe disseminated pneumonia. In one patient with pre-existing mitral stenosis there were no electrocardiographic changes suggestive of myocarditis, and it was thought that the development of cardiac failure was the cumulative result of the increased cardiac demands imposed on a heart taxed by pregnancy and pneumonia. The other two instances of congestive failure occurred in previously healthy patients with no history of cardiac disease and no physical or roentgenographic findings such as murmurs or cardiomegaly. These were thought most likely to represent acute viral myocarditis. The diagnosis was based on the finding of persistent resting tachycardia that was out of proportion to the fever and amount of pulmonary involvement, the development of a gallop rhythm, S T segment changes in the electrocardiogram, increase in heart size, and the presence of congestive failure. Two of these three patients responded to antibiotics, digitalis, diuretics, and a low salt diet, and their cardiac status seemed to improve concomitantly with the resolution of pneumonia. It is impossible to assess the precise role of the pneumonia on their cardiac failure. As mentioned previously the other patient succumbed on her third postpartum day; unfortunately permission for a postmortem examination was not granted.

Other complications in these 10 patients included the development of asymptomatic pleural effusions in four. Only one lung abscess was seen in all the 54 pneumonia cases, and this developed in one of the gravid patients with diffuse severe pneumonia. It is interesting to note that each of these 10 patients ultimately delivered full term healthy infants, in spite of the fact that many of them were desperately ill either a short time before delivery or at the actual time of delivery.

If pregnant females are omitted from the totals for adult females, one finds only 4 cases of pneumonia in 74 patients



giving an incidence of 5 per cent contrasted to 15.0 per cent in all adult females. This is more comparable to the observed incidence of 3.5 per cent in adult males.

### ROENTGENOGRAPHIC CHANGES

The roentgenographic changes in the pneumonia cases were of great interest. It was arbitrarily decided to analyze these cases by dividing them into four groups: disseminated pneumonia, bronchopneumonia, segmental pneumonia, and lobar pneumonia. Two of these terms need further definition. Segmental pneumonia was defined as the type that produced the roentgenographic appearance of lobar pneumonia but which involved only one or more segments rather than the entire lobe of the lung. The criteria necessary for the diagnosis of segmental pneumonia were that the pneumonic infiltration have a homogeneous dense area of consolidation which measured at least 3.5 cm in diameter with sharp borders and that corresponded to one or more anatomic segments of the lobe. It was sometimes difficult to distinguish between segmental pneumonia and lobular type bronchopneumonia and such cases were included in the latter group. Disseminated pneumonia was defined as pneumonic involvement of either broncho (lobular) or segmental type that involved two or more lobes which were not contiguous, that is, two or more obviously separated foci of infection.

Using these criteria, it was found that there were 11 cases of disseminated pneumonia, 36 cases with bronchopneumonic type infiltration, 6 cases of segmental pneumonia, and 1 case of lobar pneumonia. It is interesting to note that of the 11 cases of disseminated pneumonia that constituted 90.4 per cent of the total, 8 occurred in pregnant women and these cases were by far the most severe and had the most pronounced roentgenographic change. The chest films at the height of the illness in many of these women showed remarkably little aerated lung tissue remaining.

It was interesting, but not surprising, to note that the right lower lobe was the lobe most frequently affected in this series of cases (table 3). Nineteen cases of right lower lobe pneumonia occurred, three of which were segmental in type, and seven of the cases with disseminated pneumonia had involvement of the right lower lobe. Therefore, a total of 26 of the 54 patients with pneumonia had involvement of the right lower lobe (48.1 per cent). The left lower lobe was affected next most frequently with 13 cases, including the single case of lobar pneumonia. There were 6 cases of disseminated pneumonia that showed left lower lobe involvement. Therefore, this lobe was involved in a total of 19 of the 54 cases (35.2 per cent). As can be noted in table 3, the right upper lobe, right middle lobe, and left upper

lobes were least involved with 33.3 per cent, 14.8 per cent, and 7.4 per cent respectively.

TABLE 3 Distribution of pneumonia by specific pulmonary lobes

Radiographic distribution of pneumonia	All patients		Lobes involved in disseminated pneumonia	Lobes involved in all pneumonia patients	
	Number	Percent	Number	Total	Percent
Disseminated	11 (8)	20.4			
Right upper lobe	8	14.8	10	18	33.3
Right middle lobe	2	3.7	6	8	14.8
Right lower lobe	19 (1)	35.2	7	26	48.1
Left upper lobe	1	1.9	3	4	7.4
Left lower lobe	13 (1)	24.0	6	19	35.2
Total	54 (10)	100			

Number of patients with pneumonia

Follow-up roentgenograms were taken on all patients and it was found that 19 had negative findings within seven days following the height of their pneumonia. Another nine patients with bronchopneumonia had negative roentgenographic findings within 8 to 14 days. Therefore, at the end of 14 days, 28 patients (46.3 per cent of the cases) had negative roentgenographic findings. Seven patients, including four with disseminated pneumonia, required 30 to 60 days for complete roentgenographic clearing. Six patients, including three with disseminated pneumonia, still had residual markings such as fibrotic scars or pleural thickening after 60 days, and further follow-up was not obtained. Five patients did not have adequate follow-up and one patient died.

Seven patients had secondary clinical and radiographic complications, and five of these were in the disseminated group. Pleural effusion, two of which were interlobar in type, developed in six patients. Atelectasis complicated an additional four cases, and one lung abscess developed.

#### BACTERIOLOGIC EXAMINATION

Bacteriologic examination of sputum was performed in all 54 cases, and possible etiologic organisms were isolated from 19 cases. Neufeld typing was not performed on the cultures of *Diplococcus pneumoniae* and, consequently, it is impossible to state the pathogenicity of the organism in those cases in which it was isolated. The figures discussed below are presented with this fact in mind. Cultures for *Haemophilus influenzae* unfortunately were not performed. *Micrococcus pyogenes* var. *aureus* was the causative organism in 5 cases (in 4 of the 11 cases of disseminated and in 1 of the 36 of bronchopneumonia).

Sensitivity tests were determined in all cases and showed no consistent pattern. In each case the organism was sensitive to at least one antibiotic and in two cases was sensitive to three or more. Unfortunately clinical results did not always confirm the *in vivo* testing. *D. pneumoniae* was isolated in 8 cases (in 1 of 11 disseminated cases, in 3 of the 6 segmental cases, and in 4 of the 36 cases of bronchopneumonia). Beta hemolytic streptococcus was uncommon and was isolated only in 2 cases (1 disseminated and 1 segmental). No pathogenic organism was isolated in the single case of lobar pneumonia. Of great interest was the fact that *S. pyogenes* var. *aureus* was the etiologic agent in only five cases and that each of these patients was pregnant. Of the 10 cases of pneumonia occurring in the pregnant women, half of them were due to this organism. It is interesting to speculate as to the possible reasons for the prevalence of this organism in the gravid patients. These patients were isolated from the other patients with pneumonia and from each other. They were however cared for by the same hospital personnel. Inasmuch as reverse precautions were not practiced, it is possible that cross infection could have occurred among the pregnant women. If this were the case, however, one would have expected a higher incidence of pneumonia caused by this organism in the non-gravid women on the same ward. Perhaps the decreased tidal volume of air exchange, pulmonary congestion, or hormonal factors may have been primary predisposing factors underlying increased susceptibility to this organism in the gravid patient.

### SUMMARY

An analysis of 164 unselected cases of Asian influenza was made. Because of the military population studied, 89 per cent were represented by adult male patients with an average age of 23.2 years. The remaining cases were fairly equally distributed between adult females and those in the pediatric age group. Clinical symptoms, laboratory and roentgenographic findings, and the typical course in uncomplicated cases are discussed.

Complications developed in 17 cases (an incidence of 6.1 per cent) that could be attributed directly to the disease. Pneumonia occurred in 54 patients. Of particular interest was the high incidence of pneumonia (50 per cent) in gravid women and the finding that of 11 cases of disseminated pneumonia, 8 were associated with pregnancy. Bacteriologic studies made in the pneumonia cases yielded pathogenic organisms in only 19 of the 54 patients. Four of the 11 patients with disseminated pneumonia could be attributed to *Micrococcus pyogenes* var. *aureus* and all these patients were pregnant.

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#### ON NOT GIVING MEDICINES

The AMA ought to give a medal occasionally to doctors who refuse to order medicines for some of their patients! Many preparations in use today are potentially harmful and many are valueless. Many pills are prescribed but never taken. Many of the pills that are prescribed are unnecessary for restoration of the patient's well being. Except for our knowledge that patients expect them, is there any reason why we keep doling out more and more pills? Many physicians are simply too busy to sit down and explain to the patient why he does not need any medication. One young doctor spent 30 minutes explaining to a patient whose complaint was a three day old bee sting that salves were unnecessary. Subsequently he decided that if such a situation were to recur he would prescribe an innocuous salve and save himself 25 minutes. It would seem that we should honor the brave doctor who does not prescribe antibiotics for every cold and who does not give shots to every patient who complains of fatigue. Let us remember that physicians who prescribe too freely don't treat their patients; they treat themselves.

—EDITORIAL

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# THE CONFEDERATE MEDICAL OFFICER IN THE FIELD

H. H. CUNNINGHAM Ph.D.

THE organization of the field and general hospital service of the Confederate medical department was interlocking at the top level during the first two years of the war. Surgeon-General Samuel P. Moore directed the activities of each and in addition the medical directors of armies and military departments had general control over all the medical officers and hospitals within the geographical limits of their commands. It was not until March 19, 1863, that a general order was issued by the Adjutant and Inspector General's Office which altered this latter arrangement. Then general hospitals were removed from the jurisdiction of medical directors of armies and departments and placed under the authority of medical directors of hospitals.

Each army corps had a medical director who was immediately responsible to the medical director of the army. Altogether there were 18 medical directors on duty in September 1864. Medical director in addition to being generally responsible for medical officers and hospital under their control were required to prepare for the Surgeon-General two monthly reports: a consolidated report of the sick and wounded and a return of medical officer. Directly below medical directors in the chain of command came the chief surgeons of the various army divisions; these were appointed upon the recommendation of the medical director and were free from all regimental duty. Right under the division in the army's organization was the brigade and each brigade had a senior surgeon—not relieved from regimental service—to oversee its general well-being. Medical director, chief surgeon of divisions and senior brigade surgeons were directed to make such recommendations regarding the prevention of disease and the construction and economy of the hospitals and the police of the camps as may appear necessary for the benefit and comfort of the sick and the good of the service. The officers incidentally were general—not personal—

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staff officers hence they were not affected by personnel changes at the command level

Each regiment generally had one surgeon and one assistant surgeon to minister to its sick and wounded. A bill to authorize the appointment of an additional assistant surgeon to each regiment, passed by Congress in August 1861 was vetoed by President Davis on the ground that existing legislation was sufficient to meet regimental needs.<sup>1</sup> That all medical personnel did not agree may be seen in the view expressed a year later by Lafayette Guild Medical Director of the Army of Northern Virginia that every regiment should have at least two assistant surgeons. Guild also contended that senior surgeons of brigades ought to be relieved from regimental duties and that one or more assistant surgeons should be attached to each brigade as supernumeraries "for assignment to field hospitals and to supply deficiencies continually arising from sickness and death of regimental medical officers." Records kept and reports made by medical officers in the field were very similar to those required of their counterparts in the general hospitals.

General army regulations allowed regiments in the field one steward one cook and one nurse for each company. Hospital stewards appointed by the Secretary of War, performed duties similar to those executed by stewards in general hospitals. They took charge of the hospital stores supervised the cooks and nurses, and acted as medical dispensers and apothecaries. Hospital Steward George E. Waller of the Twenty fourth Virginia Regiment for example was left in charge of the field hospital during the entire winter of 1864-1865.<sup>2</sup> Nurses and cooks were usually detailed from the ranks<sup>3</sup> and a special committee appointed by the Provisional Congress to investigate the medical department complained of poor nursing and cooking in the camps. *The establishment of both an army nurse corps and a number of batteries was recommended by the committee but neither of the suggestions was deemed to be feasible.*<sup>4</sup>

Medical officers in the field were faced with many problems similar to those in the general hospitals and the regulations for the latter applied, as far as practicable to the field service.<sup>5</sup> It should be pointed out however that after the early epidemics the number of sick in the field was never so troublesome and that most of the disabled were usually transferred to the general hospitals. As a rule the most important work of field medical officers pertained to camp sanitation and caring for the men during and immediately following an engagement. Those functions will receive particular emphasis in this paper.

#### CAMP SANITATION

Regimental surgeons were responsible for finding out as much as possible about the sanitary condition of the camp site. In an

ing of diseases common to the locality and the means which had been most successful in combating them keeping a close watch over the clothing needs of the troops maintaining proper police of the encampment insisting on strict personal cleanliness enforcing all hospital regulations seeing that the water was pure and suggesting necessary dietary changes. Despite the sanitary regulations however actual conditions of camp police not infrequently manifested to use the words of a Northern observer in describing Confederate hospitals at Gettysburg a deplorable want of cleanliness and at times were disgustingly offensive. A Union army medical director examining Confederate field hospitals during the Shenandoah Valley Campaign in late 1864 reported seeing the most extreme filth and positive indications of neglect. Confederate inspectors themselves also found police regulations disregarded at times and referred to the necessity of frequent camp inspections. One inspector reported the ground surrounding a division hospital in Petersburg to be offensive to the sight as well as the smell. In this important feature of cleanliness he concluded there was evident and inexcusable neglect.

Directives concerning camp sanitation became increasingly strict as its importance became evident. A circular of the Second Brigade Second Division Army of Northern Virginia dated August 3 1862 ordered regimental commanders to publish and enforce all needful police regulations. Sinks were to be dug at once and the men were to be compelled by posted sentinels to use them. Non users were to be severely punished. A patrol in addition to the regular sentinels was to prevent the commission of nuisances within the camps. Offal was to be buried away from the camps.

Major General Moore ordered frequent inspections each month and a sanitary report to division headquarters. In the Army of Tennessee pursuant to an order of January 8 1864 the old guard was directed to clean the encampments daily while company details policed their grounds twice daily and stood in position after each policing. The brigade officer of the day was responsible for the proper placement and covering of sinks the isolation of slaughter pens the daily burning of offal the policing of places where animals were kept and for seeing that nothing offensive to decency or detrimental to health be anywhere visible. In August 1864 the Army of Northern Virginia medical director instructed chief surgeons of divisions to make at least one inspection each week of the trenches occupied by their divisions. Chief surgeons and inspectors were directed to confer and advise with the immediate commanders of troops and when deemed necessary to make such suggestions with reference to the observance of the laws of

hygiene, as will prevent disease and promote the health and comfort of the soldier "2

Naval officers commanding vessels on the Savannah River received a general order in April 1863 that clothes should be washed three times weekly and hammocks twice each month. Bedding was to be aired when hammocks were washed "2 When the army was in winter quarters there were usually regular cleaning days or "broom days " During a campaign such days took place during a lull in the fighting. On these occasions the men became almost stifled by the large clouds of dust which resulted from the sweeping and rearranging but the over all effect was probably beneficial—for the moment at least "2

Responsibility for lax sanitary practices was often assigned to commanding officers in the field. Surgeon General Moore, in a communication to the Secretary of War, dated October 18, 1861, charged regimental officers with failure to act on the suggestions of medical personnel in effectuating proper hygienic regulations and he urged that all commanding officers be directed to see that police rules were scrupulously enforced by their subordinates "2 Brigadier General Earl Van Dorn, commanding the Department of Texas in 1861, was accused of retaining Texan volunteers in an unhealthy location until practically all became diseased "2

Surgeon J. Julian Chisolm writing in 1862 excoriated commanding officers for their failure to appreciate the importance of good hygienic conditions. The Confederate Army would continue to suffer heavily from sickness and death, he contended, unless officers "take more interest in the general welfare of their men, and cease to consider professional advice often as and intrusive. The sick list " he added will offer a fair criterion of the military status of an officer and his care for taking care of his men which is one of the first principles of military science "24 Observers sometimes noticed the enforcement of sanitary measures not only red but greatly improved the discipline and spirit of the army. It was asserted that General Lee's efforts along this line formed the army which he took over from General Johnston after the latter was wounded at Fairfax. The "mutinous and dissatisfied mob into a well-disciplined fighting military machine "2 There is no question that the commanders insisted on the frequent striking and punishment of every man who refused to obey orders. The careful disposal of the excrement and the correct placement of stables and other details of the salutary results were clearly evident "2



## FIELD ROUTINES

Medical officers in the field held surgeon's call or sick call early every morning. In the Army of Tennessee sick call was made 15 minutes after reveille and the ailing of each company were marched to the hospital by a non-commissioned officer detailed daily for such duty. William H. Taylor, a medical officer, wrote of the procedure in his regiment as follows:

Diagnosis was properly made usually by intuition and treatment was with such drugs as were needed to have the knapsack and we hand it to come to. In serious cases we made an honest effort to bring to bear all the skill and knowledge we possessed but science could rarely display itself to the best advantage on account of the paucity of our resources. On the march my own practice was of necessity still further simplified and was in fact reduced to the simplest terms. In one pocket of my trousers I had a ball of blue mass and the ball of opium. All complaints were kind the same question. How a yerbawels? If they were opium I administered a plug of opium if they were but I gave a plug of blue mass.

The supply table authorized the issuance of tents for field hospital purposes but medical officers were sometimes unable to produce them. It was reported late in the summer of 1861 that because of the scarcity of tents farm houses were seeing service as hospitals all along the Potomac and the next summer General Lee requested division commanders if possible to establish their field hospitals in rented houses rather than tents. Most surgeons favored the use of tents over buildings however and some believed them to be more conducive to recovery than the general hospitals. Included among the latter group was Charles S. Tripler, Medical Director of the Union Army of the Potomac. Surgeon General Moore's sentiments on this subject were reflected during the summer of 1863 by his order that three large tent hospitals be established near Staunton and Winchester to receive all those sick and wounded from the Army of Northern Virginia who required only temporary assistance.

Medical officers in the field had a considerable amount of time on their hands when the army was not in motion and some unable to obtain professional literature and increase their knowledge of medicine in that way spent their free time writing letters seeking out attractive members of the fair sex attending religious service in the camp and promoting various other social activities. Occasionally medical societies were formed and the members thereof met to discuss medical and surgical subjects. At least one such group had a dissecting hut which was fitted up by the surgeon of a Mississippi regiment. We could easily procure subject from beyond the lines wrote a member.

of this society "and we thought it legitimate to use them for scientific and educational purposes"

### BATTLE PREPARATIONS

Careful preparations were made by medical officers in the field on the eve of expected battles. Medical Director Lafayette Guild ordered that each division medical wagon should transport 150 pairs of drawers, the same number of shirts, 50 blankets, a supply of tea and some desiccated vegetables to make soup; these items were for the use of wounded during and after a battle.<sup>39</sup> Guild pointed out, in explaining this order, that the clothing of wounded soldiers almost always had to be cut off to facilitate treatment and even when that was not the case he added, it was "improper to permit the wounded men to remain in clothes rendered offensive and stiffened with blood." Guild also explained that men suffering from wounds and loss of blood were extremely sensitive to cold even in the summer and thereby needed the warmth afforded by blankets.<sup>40</sup> It is interesting to note that many men on naval vessels removed most of their clothing prior to an engagement; other preparations on board ship included a distribution of tourniquets to division officers and a thorough sanding of the decks "to prevent slipping after the blood should become plentiful."<sup>41</sup>

The medical director of general hospitals, in close contact with the army medical director, attempted as a rule to clear all hospitals near the expected battle site of those who could bear transportation to more distant institutions and he advised the army medical director as to the number of vacant beds available in each of the hospitals under his jurisdiction.<sup>42</sup> At times, due to army movements it was necessary to relocate general hospitals. As the battle became imminent, brigade field infirmaries, identifiable by hospital flags, were established to the extent practicable; these were located in buildings outside the range of shells but strategically enough to maintain constant communication with both the front and the rear of the army.<sup>43</sup> Brigade medical personnel and supplies were sometimes consolidated for the purpose of setting up division infirmaries.<sup>44</sup>

### THE INFIRMARY CORPS

An infirmary corps comprising about 30 detailed men—usually the "least effective under arms"—and the assistant surgeon from each regiment was responsible for the care of the wounded upon the field and for the removal from the field of those unable to walk. The assistant surgeon who was in charge of the infirmary corps was to equip himself with a pocket case of instruments, ligatures, needles, pins, chloroform, morphine, alcoholic stimulants, tourniquets, bandages, lint, and splints. All members of the infirmary corps were unarmed and wore a badge to di-

Stout's department to be entirely insufficient. And in 1865 entire brigades in the Department of Western Virginia and East Tennessee were found to be without ambulances or medical wagons of any kind. Priorities assigned to the use of wagons for purposes of forage and the movement of subsistence stores during the closing weeks of the war made the problem of transporting medical and hospital supplies almost insoluble.

The wounded usually underwent a most uncomfortable trip even when ambulance transportation was available to move them from the field hospitals. Some spring vehicles were supplied early in the war but when these broke down they were replaced by ordinary wagons and as the latter moved over rough wooded country or on roads rutted by artillery and army supply trains the occupants experienced a rude jolting. Heavy downpours some times caused wagons to become mired in the mud while at the same time the wounded were drenched by the rain falling through leaky covers. Drivers were not always considerate of their charges and one officer related that he was compelled to draw his pistol on one to stop him from traveling at breakneck speed over the roughest roads.

Ambulance wagons might also be harassed by the enemy. Two ambulance trains headed south after the battle of Gettysburg were both according to Lafayette Guild attacked by enemy raiding parties. The raiders he asserted destroyed many wagons, paroled the wounded private soldiers and took with them all of the officers who fell into their hands. When the Gettysburg wounded reached Williamsport they were moved across the swollen Potomac on rafts and ferry boats, an ambulance line was then organized to Staunton which made connections with the Richmond trains. Not all however were removed to the capital. Many convalesced in the Valley hospitals.

Field medical officers of the Army of Northern Virginia were aided to a considerable extent in the removal of their wounded to the general hospitals by an organization known as the Richmond Ambulance Committee. Established in the capital during the spring of 1862 it was composed for the most part of men exempt from military duty and had an over all membership of nearly a 100 well known citizens. Headed by John Enders the committee formed itself into a military company and attempted at its own expense to attend, feed and transport the wounded to the interior hospitals. At the battle of Williamsburg (May 5, 1862) the organization had 39 ambulances on the field and it functioned effectively in almost every engagement participated in by Lee's army. Seven thousand men passed through the committee's hands at Chancellorsville (May 9, 1863) and after the battle of Gettysburg a Richmond newspaper reported that

the Ambulance Corps was in Winchester for the entire period of three weeks at the expense of many thousands of dollars to its individual members caring for the wounded facilitating their transportation and doing all possible offices of humanity "

Coordination existed between the Ambulance Committee and the medical directors of the Virginia general hospitals and the Army of Northern Virginia " Lafayette Guild and General Lee both acknowledged publicly the great obligations they were under to the committee for its valuable and humane services "

### TRANSPORTATION OF THE WOUNDED BY RAIL

As a general rule, ambulance transportation was used only to remove the wounded to nearby railroad and water connection. A good many disabled soldiers reached the Richmond hospitals in ambulances or on steamers from Drewry's Bluff, but most wounded throughout the Confederacy were transported by rail. In the decade preceding the war the Southern states had been quite active in railroad construction, and by 1860 Virginia and Georgia ranked sixth and seventh, respectively, among all the states in railroad mileage. The enterprise shown by these two states was fortunate for the Confederacy in moving its disabled troops since their strategic location caused a large share of the burden to fall upon their lines "

The movement by rail was at times a most disagreeable experience for the wounded and a trying one for medical officials. After the battle of Chancellorsville for example, Union cavalry tore up the railroad tracks in the Confederate rear and occasioned a delay of several days in the transportation of the disabled to Richmond. Unheated cars in winter also caused suffering, the wounds of a group that reached Richmond late in November, 1863 on an unheated ambulance train were almost frozen, and the Ambulance Committee "built a fire on the track" to relieve the intense suffering. It was not unusual for trains to jump the track, and the wounded often died or received additional injuries in such wrecks. A Texan who was wrecked en route to the Stout Hospital in Milledgeville Georgia, wrote "I went all through the Tennessee campaign, and I tell you that I saw no hard times and then to get nearly killed on an old car, is rather disheartening." Inspectors complained also of lack of water in the cars and the tendency of engineers to jerk the cars in starting their trains. "Another evil" wrote an inspector late in 1863 "is in the frequent and most unreasonable delays of trains loaded with sick and wounded in the present crowded and confused condition of transportation it is doubtful whether we can effect any removal of this difficulty." Such delays were indeed unavoidable and a surgeon of the Mississippi Blind Asylum Hospital in Jackson noted that some of the wounded received there were almost "in articulo mortis" when they



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viduals to Armed Forces Examining Stations for examination to determine whether those classified by Selective Service as being available for military service will meet the existing mental moral and physical standards selection for induction of those men who are acceptable and available for military service and delivery of those eligibles in accordance with the requirements of the Armed Services

Selective Service local boards furnish a certain prescreening of the individuals eligible for military service prior to forwarding them to the Armed Forces Examining Stations The purpose of this prescreening is to eliminate registrants with obviously disqualifying defects (e g paraplegic individuals et cetera) as well as those who have been established as morally unfit The next screening of regular registrants is performed at Armed Forces Examining Stations where moral mental and physical acceptability is determined under criteria established by the Armed Forces Examining Station Policy Board The Armed Forces Examining Station Policy Board established within the Office of the Assistant Secretary of Defense (Manpower Personnel and Reserve) is composed of the Director of Manpower Utilization Office of Assistant Secretary of Defense (Manpower Personnel and Reserve) as Chairman and one general or flag officer from each of the military services The Department of the Army is designated under the Armed Forces Examining Station Policy Board as the executive agent for the Department of Defense for the administrative operation and supervision of staffing of Armed Forces Examining Stations The Surgeon General's Office Army has been charged with the responsibility for the complete processing and analysis of the physical examination records of the examinees

Individuals considered unable to meet the moral standards are those with certain criminal records those who have frequent difficulties with law enforcement agencies or who have exhibited certain antisocial behavior (alcoholism drug addiction et cetera) or who have been previously discharged from military service under conditions other than honorable or for the good of the service Morally unfit individuals are considered disqualified for administrative reasons

The examinee's mental (intellectual) qualification for military service is determined by the Armed Forces Qualification Test which is a group of mental tests developed by personnel psychologists from each of the armed services These tests consist of 100 questions divided into four groups each of which is divided among items on the meaning of words arithmetical reasoning items related to forms and positions and to test the examinee's mechanical ability The questions are arranged in a progressive order of difficulty and are given to all regular registrants at Armed Forces Examining Stations by personnel psychologists During the period 1950 to 1951 the passing

score varied, but since December 1951, the passing percentile score has been 10 points.<sup>2</sup> In 1953 a mental qualification test was developed for Spanish speaking registrants examined in Puerto Rico and covers comparable questions to those in the Armed Forces Qualification Test.<sup>3</sup> Certain procedures have been established for further testing those who failed the mental test. If found qualified on additional testing and personal interview, such persons are considered as Administrative Acceptees.

Under the Universal Military Training and Service Act of 1951, the Congress provided that the minimum standards of physical acceptability should not be higher than those applied to persons between the ages of 18 to 26 in January 1945.<sup>4</sup> The Department of Defense, shortly thereafter prescribed that the physical (medical) standards contained in Army Regulations 40 115 as amended, would be utilized in determining physical acceptability by all of the military services.<sup>5</sup> The currently established physical (medical) standards for induction and initial enlistment utilized by the Army, Navy, Air Force, and Marine Corps, are contained in Army Regulation 40 503 (Physical Standards and Physical Profiling for Induction and Enlistment).

In July 1958 the 85th Congress modified Section 4a, paragraph 3 of the Universal Military Training and Service Act, as follows:

that except in time of war or national emergency declared by the Congress the standards and requirements fixed by the preceding two provisos (i.e. the passing 10 per cent score on the mental test and the physical standards applied to persons inducted between the ages of 18 to 26 in January 1945) may be modified by The President under such rules and regulations as he may prescribe

The hearings on this bill advised the Armed Services Committee that if the legislation was enacted into law, prospective inductees with a percentile score of 31 or higher on the Armed Forces Qualification Test (AFQT) would be accepted without further screening but that it was proposed to examine those who made a score of 10-31 with the Army classification battery. This battery of tests is used to identify the preinductee's aptitude for combat electronics, general maintenance, motor maintenance, clerical, general technical and radio code. Preinductees who score between 10-31 on the AFQT must score satisfactorily in two or more of these areas or they will be rejected under the new authority. Although the bill as passed gives the authority to raise existing physical standards, the Committee on Armed Services was advised that there was no present intention to raise physical standards.

#### RESULTS OF PREINDUCTION EXAMINATIONS

A total of 4,699,527<sup>6</sup> preinduction examinations were performed at Armed Forces examining stations from the beginning of the Korean conflict (July 1950) through June 1957. The overall results are presented in table 1.

TABLE 1 R lt / p d t m t /  
g t t p d f m l t ry rv  
J ly 1950 th gh J 1951<sup>1</sup>

R g tran	N mb	P t
E arn d	4 986 367	100 0
F d pt bl	3 307 677	66 3
Disq lf d	1 678 690	33 7
M d lly d qu lf d		
ly	783 598	15 7
F l d m l t t and		
m d ally d q al f d	154 726	3 1
Fail d ment l t ly	687 355	13 8
Adm t on	53 011	1 1

A breakdown of the principal disqualifying defect in term of broad diagnosis categories among registrants disqualified for medical reasons only from July 1950 through December 1951 is contained in table 2.

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Cho cr n-be	6.3	ype	4.6
E ep	1.	Othe	f b ul ry
Othe urol l d	1.6		0.9
Tube ul	1	R ul nt re l eth	1.2
l d	0.1	Oth nc l d ppo ructur	1
Othe of ct nd au	1		0
d	0.1	Mouth d d	0
k l nant ae l	1	l f l d se	4.9
h l g nc p/		Ot d d se	5
eo mphat b a-	0.0		
opo et	0	urta ry an st	3
Othe op	6.0	d nd ll lar d	2.2
hna	0	A lu	0.8
Othe l d	0.8	A y	4
et me	0	L	1
Othe nd cr	0	l l d	5.4
etabol nd al	0.2	J oot	2
lood d lood to mi	4	D orm	4.3
cu tv on	2	mp	f ee
Othe d	0.9	C l f rmat	4.3
A f hear		ur et h d h	
Ot d h ur	4.9	sr ndar	5
pair be		Othe ms ne d d	4.6
Othe d he ar d h	0.5	f ct	

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It is apparent after reviewing the principal disqualifying diagnoses at preinduction (table 2) that there are many persons in the military service who have similar or identical medical conditions and who are being successfully utilized. This is because the military services have different criteria for entry and for retention. The criteria for retention and/or disability separation for Army personnel are contained in Army Regulation 40-44 Standards of Fitness and Unfitness for Retention on Active Duty. The fact that an individual acquires one or more

physical imperfections while in the military service does not in itself under this regulation entitle him to medical separation or retirement. The fact that a person may be entitled to certain compensation from the Veterans Administration after leaving the military service by reason of having acquired a medical defect in line of duty does not in itself entitle him to medical separation or retirement. The sole criterion for existing retention standards and/or disability retirement is whether or not the patient's physical (medical) condition is such that he can or should continue to serve in the military service.

### EXISTING ENTRY STANDARDS

The current philosophy of the military services is that the public interest is best served when physical (medical) standards are maintained at the highest permissible level consistent with the manpower resources of the national economy. If in time of full mobilization the imperative need for manpower becomes a factor of overriding importance as implied by the report of The Director of Defense Mobilization,<sup>1</sup> a lowering of entry standards to the retention criteria in use at the time might be considered as a means of increasing manpower resources. The question immediately arises from many sources, "Why don't we begin inducting these people now if they are medically capable of performing military service?" Existing entry standards represent a compromise whereby various military risk appraisal factors are balanced against anticipated manpower resources. These entry standards are lower than the medical standards in effect during World War II (after 1942) when over 10 000 000 men were mobilized. The chief military appraisal factors utilized in developing existing entry standards are listed below.

#### Medical Factors

The medical officer when performing a physical examination on individuals scheduled for entry into the military service considers the anatomic and physiologic alterations and appraises the findings with reference to the individual's ability to perform some military job. He considers the anticipated sick, hospitalization, and death rates, and/or whether aggravation or progression of the medical condition is such as to preclude military service during the individual's anticipated tour of duty. Once the individual has been accepted for military service, the entry medical examination is further utilized to classify the functional capacity so that the individual may be assigned to a job within his capacity, or to assist in the maintenance or improvement of his health. From an actuarial viewpoint there is no question but that sickness, hospitalization, and possibly death rates would be increased if the military services utilized existing retention criteria in determining acceptability for entry instead of existing entry standards.

#### Nonmedical Factors

*Anticipated pension and compensation claims.* The eligibility for compensation and pensions from the Veterans Adminis-

tration and/or disability retirement from the military service is chiefly dependent upon the circumstances under which the disability arose and the character nature or degree of the disease or injury. It is necessary that the appropriate armed service concerned make a determination of the line of duty or service connection for each medical admission. The current liberal interpretation concerning line of duty and service connection is such that almost all diseases and injuries occurring while the individual is in the military service are considered in line of duty unless the injury disease or death (1) was a result of the intentional misconduct or willful neglect of the individual (2) occurred during a period of unauthorized absence or (3) was contracted or incurred while neither on active duty nor engaged in authorized training in an active or reserve status and was not aggravated by military service.

A member of the military is presumed to be in sound physical and mental condition upon entering active service. In order to sustain the presumption that disability is not service connected it must be shown by substantial evidence that the medical condition was incurred while the individual was not on active duty or engaged in authorized training in an active or reserve status. If this presumption is overcome by substantial evidence it is a further presumption that any additional disability resulting from the pre-existing medical condition was caused by service aggravation. Only specific findings of "natural progress" of the pre-existing medical condition based on well established medical principles as distinguished from medical judgment are sufficient to overcome the presumption of service aggravation. The burden of the proof in refutation of these presumptions rests therefore primarily on the Government and more specifically on the federal medical officer. The accumulation of data by the medical officer to refute these presumptions is frequently difficult or impossible.

In addition to the presumption mentioned above certain legal interpretations policies precedents and statutes have developed over the years which further liberalize and expand the original concept of line of duty which was first employed in statute law in 1799. The Veterans Administration does not necessarily honor the "line of duty" determinations made by the military services. Certain medical conditions incurred as long as two to three years after separation are held to be service connected for pension and compensation purposes e.g. tuberculosis multiple sclerosis.

It is not possible within the confines of this study to discuss or elaborate further on the many ramifications of present concept of line of duty or service connection. It is postulated however that if entry standards were lowered to the present retention criteria the pension compensation and disability retirement burden to the taxpayer would be significantly increased.

*Availability for assignment throughout the world under various environmental conditions* It is an existing policy of the Department of the Army that all individuals who are considered qualified for retention in the service are considered qualified for duty in an overseas area to perform a like job to that performed in the Continental United States. Such a policy is just as desirable during a full mobilization as it is at the present time in order to maintain flexibility of operation and rotation schedules. Persons who have a disability of a nature and degree similar to those which are disqualifying for entry at the preinduction examination would have significant assignment restrictions and would make utilization under such a policy more difficult. It is possible that none of the individuals who barely meet retention criteria could be depended upon to perform combat duties, and they would necessarily have to be used in a support or base role.

*Training* Under existing training concepts, most individuals who enter the military service undergo a period of basic training and orientation immediately after entry. Insofar as possible, all persons now in the service are expected to complete this scheduled training except for those portions which they are physically incapable of performing. It is postulated that if entry criteria were further lowered it would be necessary to maintain multiple training schedules during basic training instead of the single training schedule concept now in force since most of the persons would have an assignment restriction of one type or another.

*Attitude of individual* Statements are frequently made that physically handicapped persons have a better work record in civilian industry than do the physically able. There are no adequate statistics to compare the use of the physically handicapped against the physically perfect persons in the military service. It is an observation, however, that the performance record of those who have a physical disability is closely associated with the individual's motivation for military service and/or his will to work. It is frequently observed that the inducted soldier who has a physical disability and is poorly motivated for military service will attempt to use this as a means of avoiding undesirable assignments or, more frequently, of obtaining a discharge from the military service. The military services by effective command leadership and medical support during the early phases of training are often able to change this attitude and salvage a large proportion of such individuals.

It is the intent of this study to analyze the "Report of Medical Examination" (SF 88) on a sample of individuals found medically disqualified at the preinduction examination but who are otherwise morally and mentally acceptable to determine the percentage who would meet existing medical retention criteria. It is not within the purview of this report to comment on the disqualifications made for moral mental reasons inasmuch as

the criteria for qualification and/or disqualification are other than medical considerations

### METHODOLOGY

The Medical Statistics Division Office of The Surgeon General Department of the Army receives a copy of the Report of Medical Examination\* (SF 88) and Record of Induction (DD Form 47) of every registrant processed at the Armed Forces examining stations whether he is inducted or found disqualified for military service and in addition a copy of the Report of Medical History (SF 89) of each disqualified registrant. The Department of Physical Standards Research Walter Reed Army Institute of Research (WRAIR) requested the Medical Statistics Division to furnish them with approximately 1 000 individual records of disqualified registrants randomly selected from the records received in July 1956 and about the same number of records so selected from those received in July 1957.

Of the total number of records furnished to the Department of Physical Standards Research WRAIR 871 records were for registrants who were disqualified for medical reasons. The records of each of these medically disqualified individuals were analyzed individually on the basis of entries made on the Report of Medical Examination (SF 88) and Report of Medical History (SF 89) to see (1) if nonacceptability was in accord with Army Regulations 40-503<sup>1</sup> and (2) to determine the number who would meet the standards utilized in the Army for retention purposes. Some of the medical information contained on the SF 88 Report of Medical Examination was scanty and in such instances it was necessary to consider the individual as not meeting retention standards. An analysis of the results is given below.

### RESULTS

An analysis of the individual medical records of the 871 cases considered morally and mentally acceptable but medically unacceptable reveals that 478 of the 871 persons (54.9 per cent) would have been found fit for military service if retention standards (AR 40-504) had been utilized in determining medical acceptability at the preinduction examination instead of existing entry standards (AR 40-503). If this percentage would stand up from month to month and year to year the medical disqualification rate which averaged 15.7 per cent from July 1950 through June 1957 might be expected to be lowered to approximately 7.1 per cent. Further if the percentage salvaged in the sample was applied to the 783 598 medically unacceptable persons for the above period a manpower savings of approximately 430 000 would be made. However if this group of persons were inducted it would increase the percentage of category C personnel (1 or more 3's in the physical profile serial) from approximately 10 per cent of those who enter the Army to approximately 20 per cent.

The source of acceptability by major disease groups using retention standards instead of entry standards is contained in table 3

TABLE 3 Source of acceptability by major disease groups using retention standards instead of entry standards

Disease	Total medically acceptable (July 1956-1957 sample)	Total unsatisfactory (time to return)	Total medically acceptable (July 1956-1957 sample)
1 Cndt of bo	149	50	99
2 Nur psych tr odt	113	113	
3 Curelty sytm o			
4 Cndt of y	96	38	58
5 G tr t tnlc dt	80	28	52
6 All g dt	67	19	48
7 F lurt meth ght	63	11	52
8 C dti fer	60	13	47
9 Gntur ry dt	56	23	33
10 Skt d lll de	33	14	19
11 R pur tryd s	26	7	19
12 N mal g ant pl sm (Pl dl )	26	20	6
13 C g tll mls	25	5	20
14 Nur lg ld	5	18	7
15 E d r dmt bol	19	14	5
16 Mlg t pl m	12	12	
17 D tll	3	3	
18 If ti d par tic	3	1	2
19 D f bld d	3	2	1
20 M scell dt	1	1	
	11	1	10
Total	871	393	478

N pt bly t b d AR 40 503 ( t g try st d rd )<sup>7</sup> d  
 c pt bly r b d AR 40 504 (ret r r d d  
 Nt Wh d d l c rd l t d mor th d q lfy g c th  
 pr pl d q lfy g d f tw t l d f l f t purp An d dual  
 c d wh h d c t d d qualify g f 20/800 r c t b l t 20/20 t ye  
 d 20/200 th h d d q lfy g r p y h t d t w uld b  
 l fed pp t Nur p y h t s dt m g c pt bl ( t  
 m t g t t r t )

## DISCUSSION

Detailed discussion and analysis of entry and retention standards as applied to specific disease entities follows



### Conditions of Bones, Joints, and Muscles

One hundred and forty nine persons in the sample were disqualified at the preinduction examination because of conditions of the bones, joints, or muscles. If retention standards (AP 40-504) had been utilized instead of entry standards (AR 40-503) in determining medical acceptability of the group, 99 of the 149 could reasonably be expected to be advantageously utilized in the military service. A more detailed discussion of the standards and implications involved is given below.

**Arthritis.** Sixteen of the persons disqualified at preinduction examination were disqualified because of rheumatoid arthritis or arthritis secondary to fractures or to operations in joints. Entry standards (AR 40-503) preclude acceptance of persons who have active or subacute infectious arthritis or rheumatoid arthritis, including Marie Strumpell type. Arthritis secondary as a residual of fracture or surgical procedure is individually evaluated based on whether the resulting condition is of such a degree as to interfere with military service. Retention standards (AR 40-504) permit retention if the arthritis is relatively asymptomatic. The person is medically separated for arthritis only when limited function or persistent pain is present and if not correctible by treatment. Ten of the 16 persons disqualified by reason of arthritis were considered to meet retention criteria and capable of performing military service. Each of these 10 persons had arthritis which was traumatic in origin or secondary to a surgical procedure but was asymptomatic or relatively asymptomatic. The 6 persons who did not meet retention criteria had symptomatic arthritis due to trauma (3 persons) and/or symptomatic rheumatoid arthritis (3 persons).

**Ankylosis—limitation of motion.** Eleven persons in the sample were disqualified at the preinduction examination because of ankylosis with limitation of motion. The cause was secondary to fracture in all instances. Entry standards (AR 40-503) do not specifically mention ankylosis or limitation of motion as such. These conditions are generally acceptable, however, when the resulting deformity does not or has not interfered with function to a degree sufficient to prevent the person from following a useful vocation in civilian life. Retention standards (AP 40-04) are more specific and specify that members will not be considered for medical separation unless limitation of motion exceeds the measurements listed below.

1. Shoulder
  - a. Forward flexion to 90°
  - b. Abduction to 90°
2. Elbow
  - a. Flexion to 80°
  - b. Extension to 120°

- 3 Hip
  - a Flexion  $90^{\circ}$
  - b Extension 10 (beyond  $180^{\circ}$ )
- 4 Knee
  - a Extension to  $170^{\circ}$
  - b Flexion to  $90^{\circ}$
- 5 Ankle
  - a Dorsiflexion to  $80^{\circ}$
  - b Plantar flexion to  $100^{\circ}$
- 6 Wrist Less than a total of  $15^{\circ}$  extension plus flexion
- 7 Hand Pronation to the first quarter of the normal arc

Using the retention criteria listed above, it was determined that 6 of the 11 persons would meet retention criteria and could reasonably be expected to be utilized in some type of assignment. Assignment limitations would be indicated for all persons.

*Musculoskeletal* Thirty nine persons in the sample were disqualified because of musculoskeletal deformities. Thirteen of these persons had residuals of poliomyelitis, and 10 had a low back syndrome. The others were secondary to birth injuries or trauma. Entry standards (AR 40-503) preclude acceptance of persons who have muscle paralysis or contracture which disturbs function to the degree of interference with military service, pain in lower back or leg which is intractable and disabling to the degree of interference with the function of walking and weight bearing power. Retention standards (AR 40-504) state that persons who have sacroiliac strain, chronic, mild, will be retained in the service. Persons with residuals of poliomyelitis and/or peripheral nerve injury are evaluated on an individual basis consistent with permanence of recovery and residual functional disability. An analysis of the 39 persons so disqualified indicated that 21 of the 39 could reasonably be expected to perform military service with assignment limitations.

*Flatfoot* Ten persons in the sample were disqualified for pes planus. Entry standards (AR 40-503) preclude acceptance of persons with pronounced cases of flatfoot accompanied by decided eversion of the foot and marked bulging of the inner border due to inward rotation of the astragalus, whether symptomatic or asymptomatic. Retention standards (AR 40-504) permit retention of practically all persons with pes planus. Assignment limitation is indicated in some cases. Analysis of the 10 cases in which individuals were disqualified indicated that 7 of the 10 persons could be expected to be advantageously utilized in the military service.

*Deformities* Seventy one persons in the sample were disqualified at the preinduction medical examination for miscellaneous deformities of the upper and lower extremities and the back. Most of these conditions are residuals of trauma with 23

instances involving the knee Entry standards (AR 40-50) preclude acceptance of those with the following conditions: old ununited fractures which significantly interfere with function; old unreduced or recently recurring dislocations of any of the major joints; any disease of the hip, knee, or ankle joint which interferes with function and weight bearing power; an unstable or internally deranged joint which causes disabling pain or seriously limits function; history of surgical correction of dislocated semilunar cartilage or loose bodies of the knee for one year; knee ligaments not stable in the lateral and antero-posterior directions in comparison with the normal knee; a pathological condition shown by x-ray, x-ray, or atrophy of the thigh musculature in comparison with the normal side; less than full active motion in flexion and extension or other symptoms of internal derangement; deformities due to fracture or other injury which seriously interfere with function and weight bearing power; active or recently recurring osteomyelitis of any bone; or a substantiated history of osteomyelitis of any of the long bones of the extremities at any time unless successfully treated two or more years previously.

Retention standards (AR 40-504) permit evaluation of deformities on an individual basis and most persons are retainable with or without assignment limitations. Recurrent dislocations of large joints are generally considered retainable as they are remediable by surgery. A history of osteomyelitis *per se* is usually not considered to render a person unfit for retention. Unstable major joints may render the person unfit if symptomatic and not correctible by treatment. An individual analysis of the cases of this group utilizing retention standards indicated that 56 of the 71 persons would meet retention standards but most would have some assignment limitations (*e.g.* those with knee disorder would have to forego long marches and active vigorous sports programs).

**Imputations.** Two persons in the sample were disqualified at the preinduction medical examination because of amputation of fingers in excess of entry standards. If retention standards had been utilized in determining acceptability for military service both persons could be utilized. However they probably would have difficulty firing a rifle or performing the manual of arms.

#### **Neuropsychiatric Conditions**

One hundred and thirteen persons in the sample were disqualified at the preinduction medical examination because of neuropsychiatric conditions. Breakdown of this group is as follows: 7 with psychosis or documented history of treatment for psychosis within 5 years; 26 with psychoneuroses; 49 with character behavior disorders; 3 with mental deficiency (unable to take AFQT) and 4 with miscellaneous neuropsychiatric conditions.

Entry standard (AR 40-503) permit acceptance of all persons with neuropsychiatric conditions that have not materially in-

capacitated them in civilian life, except for persons who have an authenticated recent history of psychosis. Under this policy, if the person has acceptable mental requirements and has made a reasonable adjustment in civilian life as manifested by ability to get along tolerably with family, friends, casual acquaintances, authorities in school or society, employers, and fellow workers maintains a conventional attitude toward sexual problems, has sufficient stability and ability to obtain and keep, or at least seek a job, he will be given the opportunity for a trial of military service. While some of the persons accepted in terms of the above criteria have to be subsequently separated for medical or administrative reasons, a significant percentage of those inducted under these criteria make a satisfactory adjustment within the military service and prove that the policy is realistic.

Retention standards provide that psychoneurosis, if persistent and severe, may be considered to cause medical unfitness, provided the neurotic symptomatology is the basic reason rather than weakness of motivation and/or underlying personality disorder. Psychosis or recent history of psychosis is usually considered to render the individual unfit for further military service. Character and behavior disorders are not considered a cause for medical unfitness but may be the basis for administrative separation. This group of cases, therefore, represents a situation where the entry standards and retention standards are essentially the same. For this reason, an analysis of the 113 cases in the group did not reveal any persons who had been improperly classified at the preinduction medical examination, and further significant manpower gains from this group cannot be expected.

#### **Circulatory System Diseases**

Ninety six persons in the sample were disqualified at pre induction examination because of circulatory system diseases. If retention standards (AR 40-504) had been utilized instead of entry standards (AR 40-503) in determining medical acceptability of the group, 58 of the 96 persons would have been found physically qualified for military service. A more detailed discussion of the standards and implications involved is given below.

*Heart disease organic and valvular.* Thirty seven persons in the sample were disqualified by reason of organic and/or valvular heart disease. This does not include persons disqualified for congenital heart conditions which are reported under congenital malformations. Entry physical standards (AR 40-503) preclude acceptance of persons who have acute rheumatic fever or verified history of a single attack within the previous two years or recurrent attacks of rheumatic fever at any time. Valvular heart disease, documented angina pectoris, authenticated history of coronary thrombosis and/or myocardial infarction, circulatory failure manifested by definite symptoms and/or evi-

dence of congestive failure hypertrophy and/or dilatation of the heart

It is the intent of these entry standards to exclude from active military service any person affected with disease of the heart which impairs his ability to undergo severe bodily exertion. Many men with compensated heart disease are able to undergo severe bodily exertion but the question of aggravation by military service especially by activation of rheumatic carditis is likely to arise and incidentally to create compensation and pension problems. Therefore under existing entry standards all individuals with valvular heart disease are rejected for military service. From an actuarial standpoint these standards are realistic and in accord with the policy followed by most insurance appraisers.

Retention standards (AR 40-504) permit retention of persons who acquire valvular heart disease in the military service if asymptomatic. Those with symptomatic heart disease are usually separated through medical channels. As a general policy, those who have a documented symptomatic acute myocardial infarction usually are not retained in the military service for unrestricted military duty.

Exceptions to this policy are made dependent upon the absence of significant complications and residual findings and the desire of the person to return to duty after being properly informed of the hazards of prognosis. Those who have no history of cardiac symptoms and/or positive physical signs past or present but who during the course of a routine physical examination exhibit an abnormal electrocardiogram consistent with the residuals of a healed myocardial infarction are generally continued in the military service. If subsequent study and follow up evaluation reveals further cardiac deterioration on the electrocardiogram or other positive symptoms or findings of coronary or myocardial insufficiency the person usually will be medically separated even though there has never been a positive history or documented findings of an acute myocardial infarction.

Asymptomatic persons whose only finding consists of abnormalities demonstrated by the electrocardiogram such as low voltage or negativity of the T waves or an abnormal response in the postexercise electrocardiogram (positive Master's tests) are usually retained in the service as a general policy inasmuch as the determining criterion for retention is the presence or absence of clinical coronary insufficiency of such severity as to produce disability.

The cause of 93 of the murmurs was reported to be rheumatic in origin. In the remainder the cause could not be determined. The appraisal of a heart murmur based on the recorded impression of unknown medical examiners on the report of pre-induction medical examination in these instances was extremely difficult and further evaluation by qualified cardiologists

ogists would certainly be indicated prior to making a determination of acceptance for military service. Analysis of the disqualifications within these limitations indicated that 18 of the 37 individuals disqualified met retention standards and could reasonably be expected to be utilized in the military service with or without assignment considerations. All the persons who were considered to meet retention standards were asymptomatic. Many of the persons did not know that they had a heart murmur prior to the preinduction examination. None of the group had any evidence of associated hypertension or cardiomegaly. It is doubtful if any of these persons would be accepted by insurance medical appraisers. It is postulated that the majority of the group could perform military service without aggravation over and above that which would occur to them if they had continued in civilian life.

*Hypertension.* Fifty-one persons in the sample were disqualified at the preinduction examination by reason of hypertension. Entry physical standards (AP 40-503) preclude acceptance of individuals who have persistent blood pressure at rest above 150 mm Hg systolic or above 90 mm Hg diastolic. Elevation of blood pressure from excitement proved to be temporary in nature is acceptable. Retention standards (AR 40-504) provide that persons with a variable blood pressure of 150-180 and 100-110 (early or mild hypertension) occasionally elevated above these limits under stress but almost always falling to near normal (140/90) with rest, sedatives, or anti-hypertensive drugs with no changes or minimal changes in the fundi and/or minimal or no changes in the heart and kidneys will be considered qualified for retention. Occasionally, an individual will be retained who has higher blood pressure levels which will return to normal limits with rest, sedatives, or antihypertensive drugs. Hypertension associated with radiologic evidence of definite cardiac enlargement or with a history of cardiac decompensation or with retinal findings indicative of a malignant hypertension is considered to render the individual unfit for further retention.

Analysis indicated that 35 of the 51 individuals disqualified at preinduction examination did meet retention standards and could reasonably be expected to be utilized in the military service. All of the persons considered to meet retention standards had hypertension of the mild or early type (150 to 180 mm Hg systolic, 90 to 110 mm Hg diastolic), were asymptomatic and there was no recorded evidence of heart, kidney, or fundi changes. Because of the age of this group (under 26 years), it is postulated that most of the persons could reasonably be expected to complete a tour of military service of two to five years without the possibility of incapacitating progression. Progression of signs and symptoms would, no doubt, occur in many instances to the degree that the person would be eligible for Veterans Administration compensation and pension benefits.

*Other circulatory system diseases* Eight persons of the sample were disqualified at preinduction examination for other circulatory system diseases 1 for complete heart block 1 for frequent premature ventricular beats 1 for recurrent paroxysmal tachycardia 3 for simple tachycardia 1 for varicose veins of a marked degree and 1 for recurrent thrombophlebitis Entry standards (AR 40 503) preclude acceptance of individuals who have a pulse rate of 100 or over which is persistent in the recumbent position unless due to psychic reaction or secondary to other diseases when the cause will be the determining factor concerning qualification Paroxysmal tachycardia if recurrent and disabling is disqualifying for entry as is heart block of a significant degree (a slight increase in the P R interval of the electrocardiogram in the absence of other evidence of heart disease does not necessarily disqualify for entry) any serious disturbance of rhythm such as auricular fibrillation is disqualifying Thrombophlebitis or chronic venous insufficiency resulting from thrombophlebitis of one or more extremities is disqualifying for entry Other abnormalities of the peripheral vascular system including large varicose veins Raynaud's disease thromboangitis obliterans erythromelalgia and arteriosclerosis are also disqualifying for entry

*The person who has a cardiac arrhythmia which is present* in a mild degree and is discovered at a routine examination not because of symptoms is usually retainable especially when the arrhythmia is unaccompanied by any other evidence of cardiovascular abnormality The person who has an abnormal electrocardiogram with features diagnosable as a bundle branch block as the only objective or subjective finding is ordinarily retainable in the service Simple tachycardia in itself is seldom a cause for medical separation The three persons who had a simple tachycardia the individual with heart block and the one with premature ventricular beats were considered to meet retention standards

Recurrent phlebitis residuals of phlebitis such as persistent edema ulceration or claudication which interferes with the performance of acceptable military duty may be a cause for medical separation Varicose veins usually are not a cause for medical separation inasmuch as a large percentage are remediable by various surgical procedures When the deep veins are inadequate or when residuals of varicose veins including recurrent dermatitis or ulceration symptomatic edema extensive scarring or pigmentation of the skin or other physical defects prohibit surgical correction the individual may be found unfit for retention

#### Disabilities of the Eye

Eighty persons in the sample were disqualified at the preinduction medical examination because of diseases of the eye

If retention standards (AR 40 504) had been utilized instead of entry standards (AR 40 503) in determining medical acceptability of the group 52 of the 80 persons would have been found acceptable for military service. A more detailed discussion of the standards and implications is listed below.

*Visual defects* Fifty persons of the sample were disqualified because of visual defects. Entry standards (AR 40 503) preclude acceptance of persons whose refractive error exceeds 20/400 in each eye without glasses, except that persons who have a minimum vision of 20/400 in each eye without glasses are acceptable if correctible to 20/40 in one eye and 20/70 in the other eye or 20/30 in one eye and 20/100 in the second eye or 20/20 in one eye and 20/400 in the second eye provided the defective vision is not due to active or progressive organic disease. In addition, persons with any degree of defective vision in one eye from below 20/400 to no light perception, may be accepted provided the defective vision is not due to active or progressive organic disease and the vision in the second eye is not less than 20/100 correctible to 20/20 with glasses. Retention standards (AR 40 504) provide that persons will be retained with any degree of uncorrected vision whenever the eye condition present can be corrected in the better eye to at least, 20/40 provided the defective vision is not due to active or progressive organic disease.

Analysis indicated that 39 of the 50 persons disqualified for visual defects would meet retention criteria. The defective vision in most instances was due to myopia. Inasmuch as the Veterans Administration does not consider defects of form or structure of the eye of congenital or developmental origin such as regular astigmatism, myopia (other than malignant or pernicious), hyperopia and presbyopia as compensable conditions it seems that this group of conditions represents an over productive of manpower without significant expectancy of increased cost to the taxpayer. Assignment limitations would be indicated in practically all cases.

*Other eye conditions* Thirty persons of the sample were disqualified at the preinduction medical examination for miscellaneous eye conditions. Entry physical standards (AR 40 503) preclude acceptance of persons who have loss of one eye or diseases of the eye such as glaucoma, malignant tumor, exophthalmos sufficient to interfere with proper closure of the eyelids and protection of the cornea, diplopia from any cause or of any degree, any tumors of the orbit and abnormal conditions of eyes or visual fields because of diseases of the brain, nystagmus if true and persistent, permanent and well marked strabismus (over 20° deviation) or any degree of strabismus if accompanied by diplopia, opacities of the lens, presumably progressive or dislocation of a lens, acute, chronic,



or recurrent inflammation of the uveal tract (iris ciliary body or choroid) retinitis uveitis neuroretinitis optic neuritis papilledema bilateral optic atrophy pigmentary degeneration of the retina or detachment of the retina or any other organic disease of the eye not mentioned above which threatens continuity of vision or impairment of visual function

Retention standards (AR 40 504) permit retention of persons with the following conditions except as noted history of detached retina if the retina has become reattached and residual vision is not less than the retention visual standards mentioned above or the visual field is not damaged so that its greatest diameter is less than 20 retinitis pigmentosa unless there are sufficient objective findings in the retina and optic nerve and unless residual visual acuity exceeds retention criteria mentioned above or the visual field is constricted to less than 90 in diameter cataracts unless visual loss is in excess of that described above glaucoma in its incipient stage vitreous floaters unless extremely severe and the source of severe asthenopia nystagmus macular degeneration choroiditis optic neuritis vitreous hemorrhages retinal hemorrhages keratitis traumatic hole in the macula keratoconus unless visual field and vision fall below the limits described above

Analysis indicated that 13 of the 60 persons disqualified were found to meet retention criteria The range of miscellaneous eye disease included 8 persons with anophthalmos associated with trauma who were fitted with prosthesis 8 with strabismus exceeding 90 3 with cataracts 1 with dislocated lens 1 with permanent nystagmus 1 with reattached retina 1 with chronic iridocyclitis 1 with chronic choroiditis and 1 with recurrent corneal ulcer All of those found to meet retention criteria would require assignment limitations

#### Gastrointestinal Diseases I I d g H r n f Abdominal Cavity

Sixty seven persons in the sample were disqualified at preinduction examination because of gastrointestinal disease including hernia of the abdominal cavity If retention standards (AR 40 504) had been utilized instead of entry standards (AR 40 503) in determining medical acceptability of the group 48 of the 67 would have been found physically qualified for military service A more detailed discussion of the standards and implications involved is given below

*Hernia of abdominal cavity* Thirty one persons of the sample were disqualified for inguinal hernia which descended into the scrotum Entry physical standards (AR 40 503) specify that inguinal hernia which descends into the scrotum recurrent hernia postoperative hernia ventral and umbilical hernia if moderate or large in size are disqualifying whereas retention standards (AR 40 504) specify that those with hernias which are considered correctible by surgery will be considered qualifi-

fied for retention in the military service Retention standards further specify that individuals who refuse surgery for hernias are to be utilized, if possible, in some military job for which qualified Two or more recurrences of hernia which occur in the same location require individual consideration based on the degree and extent to which the hernia incapacitates

Analysis indicated that 29 of the 31 persons disqualified for hernia met retention standards and could reasonably be expected to be utilized in the Army whether operated on or not operated on after induction If the retention policy concerning hernias were adopted it is anticipated that a large percentage of the group would accept an operative procedure which would, after appropriate treatment and convalescence make them available for unrestricted assignment, provided they did not have additional complicating medical conditions Inducted persons with hernia who would not agree to surgical operation would probably require a truss and/or assignment restrictions

Implementation of such a policy would create a significant burden on the Armed Forces medical services and would probably cause noneffective time of approximately four to six weeks for each person operated on It might be desirable to consider authorizing the surgical repair by local physicians or at the nearest Veterans Administration facility for those who would consent to the surgical procedure prior to induction Such a policy would eliminate the noneffective time had they been operated on within a military hospital and would relieve the burden on medical facilities and resources It is not anticipated that pension and compensation claims would be significantly increased if persons with hernias were routinely inducted and/or operated on within the military service This medical condition (hernia of the abdominal cavity) represents therefore a segment of manpower that could be advantageously utilized by the military services without assuming too many liabilities

*Peptic ulcer* Twenty six persons of the sample were disqualified for peptic ulcer (duodenal ulcer) at the preinduction medical examination Entry physical standards (AR 40 503) preclude acceptance of persons for enlistment or induction if there is an ulcer of the stomach or duodenum as confirmed by usual laboratory procedures or if there is an authentic history of ulcer of the stomach or duodenum

Retention standards (AR 40 504) specify that gastric and duodenal ulcer may render the individual unfit, depending on the circumstances When an ulcer develops while a person is on active duty the existing policy at most medical installations is to return the individual for a trial of duty when the ulcer heals and there is no roentgenographic evidence of a niche or crater The ulcer diathesis with simple scarring usually is not considered sufficient in itself to render a person unfit When

there are documented repeated recurrences of the ulcer and/or when persistent symptoms occur after adequate medical treatment and/or if obstruction perforation or bleeding occur consideration on an individual basis is necessary. Generally persons with these complications unless well motivated for service and/or unless the person has good insight into his problem plus understanding of the general nature of ulcer disease will be found unfit for further service. Analysis indicated that 16 of the 26 persons disqualified because of ulcer would meet the retention criteria listed above.

Peptic ulcer is one of the chief medical causes for prolonged hospitalization in the military service and is a frequent reason for separation from the service. If persons who have a documented history of peptic ulcer are inducted it is believed that compensation claims filed with the Veterans Administration will be greatly increased because a significant percentage may reasonably be expected to have one or more occurrences during their tour of military duty. Most ulcer patients in the military and/or civilian life are placed on a rigid or selective type of diet incident to their therapy. It is not practicable within the military service to maintain special diets at all the unit messes where persons who have peptic ulcer will subsist. Some program of education, diet selection and periodic follow up such as that suggested by Palmer, Sullivan and Hamilton, Sullivan and Hamilton, Jastremski and Heffernon, and Wise and associates would be necessary to overcome this deficiency. It is postulated that the medical discharge rate would be increased as would noneffective time for the group as a whole but a significant percentage could probably complete their tour of inducted service if intelligently handled by medical officers, assignment officers and commanders.

*Other gastrointestinal diseases.* Ten persons of the sample were disqualified at the preinduction medical examination because of miscellaneous gastrointestinal diseases. Four had evidence of recurrent intestinal obstruction and met neither retention nor entry standards. Two persons were disqualified for ulcerative colitis and one for regional enteritis and met neither entry nor retention standards. Three of the 10 persons disqualified are considered to meet retention standards: one had mild residuals of cholecystectomy and two were convalescent from acute hepatitis but were expected to show complete recovery and availability for unlimited assignment in two to three months.

#### Allergic Diseases

Sixty three persons in the sample were disqualified at preinduction examination because of allergic diseases. If retention standards (AR 40-504) had been utilized instead of entry standards (AP 40-03) in determining medical acceptability of the

group 52 of the 63 persons probably would have been found qualified for service with the Army. A more detailed discussion of the standards and implications involved is given below.

*Asthma* Sixty persons of the sample were disqualified for asthma. Entry physical standards (AR 40 503) specify that a history of bronchial asthma is disqualifying for entry except for persons who had a childhood asthma with a reliable history of freedom from symptoms since the twelfth birthday. Retention standards (AR 40 504) specify that those with asthma or other allergic diathesis which is mild in nature or, if seasonal or readily controlled by oral medications or by desensitization are qualified for retention in service. If these retention standards were utilized in medically evaluating the individuals disqualified for asthma 50 of the 60 persons would have been found qualified for military service. The 50 found meeting retention criteria had asthma of a mild nature, the attacks were infrequent, not causing hospitalization, and were amenable to therapy. If such a group were inducted it is anticipated that modification of basic training schedules would be necessary for some of the persons inasmuch as the environment encountered during basic training might be expected to precipitate attacks of asthma. It is further anticipated that hospitalization and disability separations among this group would be increased and that pension and compensation claims subsequently would be expected for most of the group under existing eligibility criteria utilized by the Veterans Administration. This group does represent a segment which would be productive of manpower provided the cost to the taxpayer in increased hospital admissions and compensation claims is not considered to be an overriding factor.

*Other allergic diseases* Three persons with other allergic diseases (one had a documented allergy to meat, and two had hay fever, severe) were disqualified at the preinduction medical examination. Entry standards (AP 40 503) specify that hay fever if severe is unacceptable but mild or moderate hay fever is acceptable. Retention standards (AP 40 504) provide that individuals with hay fever will be retained provided the condition is readily controlled. The two hay fever cases in this instance were under control by medication appeared to be of a moderate rather than severe degree and were considered to meet the criteria established for retention.

#### **Failure to Meet Height and Weight Standards**

Sixty persons in the sample were disqualified at preinduction examination because of failure to meet height and weight standards. If retention standards (AP 40 504) had been utilized instead of entry standards (AR 40-503) in determining medical acceptability of the group 47 of the 60 disqualified persons would have been found physically qualified for military service.

A more detailed discussion of the standards and implications involved is given below

*Obesity* Thirty eight persons of the sample were disqualified at the preinduction examination because of obesity. The entry standards (AR 40 503) regarding overweight prior to 27 March 1957 were not rigid but were left essentially to the discretion of the examining medical officer. Under these criteria if the height weight relationship was not so excessive as to interfere with military training the person could be accepted. Changes No 2 Army Regulation 40 503 27 March 1957 modified this policy and specified that persons who are 15 per cent or more over the maximum weight outlined in paragraph 13 Army Regulation 40 105 (about 30 per cent over average weight) would not be found qualified by medical examiners of Armed Forces examining stations but that the records would be referred to the Army commander for review and for decision regarding acceptability. After the latter policy was placed in effect the medical rejection rate for obesity increased significantly. Retention standards (para 13 AR 40 504) rarely consider a person unfit for retention by reason of obesity alone.

Analysis indicated that 30 of the 38 persons disqualified for obesity would meet retention criteria and could reasonably be expected to be advantageously utilized. The significance of obesity in the younger age group is not well established. If however the overweight condition is long standing or is in association with such conditions as elevated blood pressure, diabetes or albuminuria the morbidity and mortality may be expected to increase as aging progresses.

*Underweight* Twenty persons were disqualified at the preinduction examination because of underweight. Entry standards (AR 40 503) specify that the minimum weight for induction is 105 pounds except that the minimum weight for Filipinos, Puerto Ricans and persons of Oriental descent is 101 pounds. Retention standards (AR 40 504) do not specify any minimum weight. Five of the 20 persons who were disqualified for underweight were Puerto Ricans and one was a professional jockey who intentionally maintained a low weight. If retention standards were utilized in determining qualification for military service, 15 of the 20 disqualified at preinduction examination could be expected to be advantageously utilized. Poentgenograms of the chest of the 15 persons meeting retention standards were without evidence of associated disease.

*Height* Two persons in the sample were disqualified by reason of being overheight. Entry standards (AR 40 503) specify that persons below 60 inches in height or over 78 inches will not be accepted for military service. Height standards (AR 40 504) are not used as criteria for retention and in fact height alone is usually not considered as a medical appraisal factor.

The height weight relationship however, is of medical significance. The two persons disqualified had no evidence of disease the height weight relationship was satisfactory, and they were considered to meet retention standards.

### Diseases of the Ear

Fifty six persons in the sample were disqualified at the preinduction medical examination for diseases of the ear. If retention standards (AR 40 504) had been utilized in determining medical acceptability of the group 33 of the 56 persons would have been found qualified for military service. A more detailed discussion of the standards and implications is given below.

*Defective hearing* Twenty five persons in the sample were disqualified because of defective hearing. Entry standards (AR 40 503) preclude acceptance of individuals whose audiometric average loss for each ear exceeds 25 decibels (no loss greater than 30 decibels) at each of the frequencies 500, 1 000 and 2 000 cycles per second and/or over 60 decibels (no loss greater than 70 decibels) at each of the frequencies 4 000 and 8 000 cycles per second. Retention standards (AR 40 504) specify that no Army member will be found unfit for retention on active duty solely because of hearing defect, provided such hearing defect can be improved by the use of a hearing aid to a loss of 20 decibels or less in speech reception score. It was impossible based on the recorded information on the "Report of Medical Examination" to determine which persons could be benefited by a hearing aid and thus meet retention criteria. Six of the 25 had hearing in one ear of such a degree as to meet retention criteria. It is possible that more individuals in this group could be salvaged, provided detailed hearing evaluation by an otolaryngologist is made.

*Otitis media* Thirty one persons in the sample were disqualified at the preinduction medical examination because of chronic otitis media without hearing loss. Entry standards (AR 40 503) preclude acceptance of individuals at the preinduction medical examination who have acute or chronic suppurative otitis media, chronic catarrhal otitis media, or acute or chronic mastoiditis. Retention standards (AR 40 504) specify that otitis media will not be considered to render a person unfit for retention unless the disease becomes chronic suppurative, is resistant to treatment, requires frequent hospitalization and is at least moderate in severity. Twenty seven of the 31 persons disqualified at preinduction medical examination are considered to meet retention criteria.

### Diseases of the Genitourinary System

Thirty three persons in the sample were disqualified at the preinduction examination because of diseases of the genitourinary system. If retention standards (AR 40 504) had been

utilized instead of entry standards (AR 40 503) in determining medical acceptability 19 of the 3 persons disqualified would have been found qualified for military service A more detailed discussion of the standards and implications involved is given below

*Albuminuria* Twenty one persons in the sample were disqualified by reason of albuminuria and/or evidence of nephritis latent or active Entry standards (AR 40 503) preclude acceptance of persons with evidence of acute or chronic nephritis or persistent albuminuria Mild albuminuria without casts which is proved by observation and repeated examination to be temporary in character or orthostatic in type is not disqualifying Instructions to medical examiners state that when albumin and/or casts are found in the urine urinalysis should be repeated not less than twice a day for two or more successive days If the urine consistently shows albumin and/or casts and is associated with enlargement of the heart hypertension and other evidence of cardiovascular renal disease the person will be disqualified If the albumin/casts/blood are not constant and are not associated with evidence of cardiovascular and/or renal disease decision regarding acceptance is left to the judgment and discretion of the medical examiner Retention standards (AR 40 04) specify that albuminuria *per se* will not be considered a reason for medical unfitness Those with glomerulonephritis of a mild degree are retainable Analysis indicated that 11 of the 21 individuals disqualified for albuminuria or glomerulonephritis would meet retention standards and could reasonably be expected to be utilized in the military service Each of the 11 persons determined to meet retention standard had normal blood pressure and was asymptomatic

*Veneral disease* Two persons were disqualified at the pre induction examination for venereal disease one for acute gonorrhea with doubtful serologic test for syphilis and one who had a positive serologic test for syphilis These conditions are not in themselves ordinarily considered as a cause for disqualification for entry and actually these individuals should not have been disqualified They should have been qualified and reported to the local health authorities for treatment and called up for induction when treatment was completed If treatment was not taken as scheduled the individual should have been inducted and treated in the military service

*Other genitourinary conditions* Ten persons were disqualified for miscellaneous genitourinary conditions 2 for hydronephrosis 1 for hydrocele 1 for nephrectomy 1 for symptomatic undescended testicle 1 for varicocele 1 for kidney stone recurrent 2 for prostatitis Entry standards (AR 40 503) preclude acceptance of persons with hydronephrosis or pyonephrosis nephrectomy undescended testicle which lies in the inguinal

canal when symptomatic, hydrocele if large, varicocele if large or painful, presence of renal calculi, or substantiated history of bilateral renal calculi at any time. No mention is made in entry standards regarding prostatitis other than the generalization that persons with acute pathologic conditions from which in the natural course of the disease, recovery is expected without sequelae will be found unacceptable until a subsequent examination shows recovery has occurred without disqualifying sequelae. Retention standards (AR 40 504) specify that prostatitis does not render the person unfit for retention, that nephrectomy for traumatic pyelonephrotic, hydronephrotic or nonfunctioning kidney or the congenital absence of a kidney will not render the person unfit for retention provided the remaining kidney is normal. Those with varicocele, hydrocele, and undescended testicle lying in inguinal canal are qualified for retention because they are remediable conditions. Renal stones do not usually disqualify for retention if they can be removed unless the person has had previous calculi and both kidneys are involved. Unilateral hydronephrosis is not disqualifying for retention provided the other kidney is normal. Six of the 10 persons disqualified at preinduction were considered to meet retention standards.

### Diseases of Skin and Cellular Tissue

Twenty six persons in the sample were disqualified at preinduction examination because of diseases of skin and cellular tissue. If retention standards (AR 40 504) had been utilized instead of entry standards (AR 40 503) 19 of the 26 persons would have been found qualified for military service. Entry standards (AR 40 503) preclude acceptance of those with the following conditions: chronic skin disease; chronic ulcers of the skin; or cured syphilitic lesions which are so severe as to incapacitate the individual for military service and/or so disfiguring as to render him objectionable in common social intercourse; extensive deep or adherent scars which interfere with muscular movements or with wearing of military equipment or which show a tendency to break down; generalized dermatitis of long duration; allergic dermatitis if severe; ringworm infection if very severe and not easily remediable; psoriasis if other than mild; cysts and benign tumors of the skin and of such size and/or location as to interfere with the normal wearing of military equipment; plantar warts on weight bearing areas which have materially interfered with following a useful vocation in civilian life; chronic or severe acne particularly when the face is involved to the extent of being markedly disfiguring, or the shoulders are extensively involved, making them likely to be aggravated by shoulder straps or packs or by wearing other military equipment. Entry standards (AR 40 503) do permit the acceptance of most skin conditions which are mild in nature.



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### MEDICAL MEETING—CELESTIAL STYLE

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### —EDITORIAL

Th C d M d l A t J ur l  
 P 276 A R 15 1958



## Clinicopathologic Conference

U S Naval Hospital San Diego Calif \*

### FEVER AND HEART FAILURE

**Summary of Clinical history** This 20 year old Caucasian was admitted to this hospital on 8 March 1955. He had been well prior to 2 March, when he developed an erythematous eruption on his face and a continuous frontal headache and sore throat. Two days later he noted malaise and general aches and pains particularly in his legs. He complained of occasional chilliness and sweats and for two weeks prior to admission he had a cough productive of white sputum. Upper chest discomfort was a prominent symptom for several days prior to admission. Past medical history revealed a "similar episode" at about age eight years. The systems review revealed that the patient had had minor symptoms referable to the biliary tract.

**Physical Examination** The patient was a well developed, fairly well nourished but moderately dehydrated young man who appeared lethargic and toxic. His temperature was 104 F, his pulse was 118 and his respirations were of a rapid Kussmaul type. There was white desquamation of the skin of the face and trunk. Anterior cervical lymph nodes were slightly enlarged. The tongue, roof of the mouth, buccal mucosa and pharynx were covered with a gray white material which seemed to be extremely viscid salivary secretions. Auscultation of the chest revealed fine moist rales in both lung fields, particularly at the bases. No heart murmurs were heard. The abdomen was diffusely tender and there was muscle guarding. Bowel sounds were hyperactive. The remainder of the physical examination was essentially normal.

Capt. Allen S. Chama MC USN Commanding Officer  
S. Capt. John S. Sh MC USN Chief of Staff  
Medical School Building

**Laboratory Studies** The hematocrit was 47 ml per 100 ml and the sedimentation rate was 39 mm per hour (corrected). White blood cell count was 74,600 per  $\mu$ l with 90 per cent neutrophils, 5 per cent lymphocyte and 3 per cent band forms. A repeat blood cell count the next day revealed a leucocytosis of 125,000 per  $\mu$ l while other values were unchanged. Admission urinalysis was negative but following catheterization on the fourth hospital day 3 plus albumin and many red blood cells were noted.

Poentgenograms of the chest showed an inflammatory density along the right cardiophrenic angle compatible with early bronchopneumonia.

An electrocardiogram showed a moderately low ventricular voltage with low amplitude T waves in aVL and aVF; the interpretation was suggestive of left ventricular strain.

Febrile agglutinins (including Widal) blood stool and urine cultures were all negative. Neither sputum nor throat culture was obtained.

**Course Hospital** The patient was placed on bed rest and isolation and started on procaine penicillin 1,200 mg (1,200,000 units) per day, streptomycin sulfate 10 grams per day and gantrisin, 40 grams per day. Fluids were given intravenously. During the first 24 hours the patient had approximately ten loose stools. Despite therapeutic measures he remained toxic. A surgical consultant believed that the abdominal problem was related to fluid and electrolyte imbalance. After electrolyte replacement the following serum values were obtained: sodium 139 mEq per l, potassium 1 mEq per l and chlorides 103 mEq per l, carbon dioxide combining power 43 volumes per 100 ml. Despite further rehydration, restoration of electrolyte balance and antibiotic therapy the patient remained unimproved and his tachypnea and tachycardia persisted.

On the third hospital day cyanosis responded promptly to nasal oxygen; as noted chest examination was however unchanged. At this time oliguria was found and there was no response to catheterization. Chloramphenicol was begun because of the failure to respond to previously given antibiotics.

On the fourth hospital day increasing moist rales were heard in the lungs. Cheyne Stokes respiration began and the patient became comatose. He was rapidly digitalized and tourniquets were applied to his extremities.

On the fifth hospital day the patient was started on ACTH and cortisone but he died soon after.

## DISCUSSION

Do t r Gorsu h I should like to go through the protocol and attempt to interpret some of the salient points in order to make some general izations on which to base a reasonable differential diagnosis The patient is a young man who seemed perfectly well prior to 2 March 1955 I feel reasonably sure that he had no chronic debilitating disease such as diabetes which might account for this acute episode He is said to have developed an erythematous skin eruption over his face I would wonder whether this was a broad erythema perhaps suggestive of scarlet fever or whether it was the malar erythematous eruption of lupus erythematosus His symptomatology included frontal headaches sore throat aches and pains chills and fever and cough He had upper chest pain I would have hoped the chest pain description might have been more specific Lateral chest pain aggravated by respiration with pneumonia at least is characteristic of bacterial pneumonia with pleural involvement Retrosternal chest pain seems more typical of a viral etiology Physical examination showed the patient to be lethargic toxic and febrile with a marked tachycardia and respiration of a Kussmaul type Kussmaul's respiration is commonly seen in severe dehydration and acidosis Examination of the skin revealed a white desquamation of the face and trunk we shall later return to this His lymph nodes were enlarged and the mouth showed injection viscous secretions and a gray white exudate All this suggests some sort of mouth and throat infection Chest examination showed fine moist rales in both lung fields while abdominal examination revealed tenderness The absence of cardiac murmurs or peripheral edema tends to rule out a primary cardiac etiology for this man's illness

In general terms this represents a young man who over a two week period developed a facial erythema and signs of some type of infectious prodrome with excellent evidence for an upper respiratory infection Later he seemed to develop a severe bacterial pneumonia severe because he was dehydrated lethargic and toxic It resembled a bacterial infection because the patient had high fever tachycardia and tachypnea and the patient's very toxicity suggests a bacterial invasion This probably was a pneumonia because the patient's main trouble seems to have been a productive cough chest pain and tachypnea and he was noted to have bilateral rales on physical examination At this time no other organ system is implicated It seems reasonable to assume that we have at least what seems to be a severe bacterial pneumonia

Going back we see that the patient's white blood cell count was elevated to 27 000 with a shift to the left and that his urinalysis was negative I should like to make a point of the negative admission urinalysis because I think that the later finding of albumin and red blood cells was probably secondary to the initial process and not a

part of the primary diagnosis. A roentgenogram of the chest and an electrocardiogram were taken on admission and we shall have the reports now.

**Dr. York:** There is a well defined peribronchial pneumonia in the right cardiophrenic angle. Findings are consistent with a bronchopneumonia in the right base. There is a general thickening of the lung fields bilaterally although no other infiltrate is seen. The findings are definitely abnormal but non-specific.

**Dr. R:** Electrocardiograms were obtained on this patient on three successive days (9, 10, and 11 April 1955). The tracings are basically similar and are characterized by a marked sinus tachycardia, low amplitude, and a poorly delineated T wave over the lateral precordial lead. The echogenic area slightly more marked on the tracing of 10 April 1955, which is definitely bilateral. The change are considered nonspecific but could be compatible with underlying myocarditis.

**Dr. G:** I feel sure that most of the electrocardiographic changes are entirely specific and represent a toxic state.

The patient was treated with large doses of penicillin, streptomycin sulfate, and gentamicin and within the first 24 hours his condition improved. Was there any relationship between the diarrhea and the antibiotics? With the diarrhea he developed dehydration and abdominal pain. The surgeon believed that his abdominal pain was caused primarily by dehydration yet despite rehydration and electrolyte replacement the patient deteriorated.

Several other points deserve comment at this time. First, the x-ray findings are minimal and less than one would expect with such a toxic state. Possible explanation is twofold. One is that pneumonia is not the primary cause of the toxic state but rather that it is a reflection of some other process such as dehydration and acidosis. Another possibility is that there is considerably more pneumonia than the lung shows. The x-ray indicated Physiological pneumonia. I did feel some trouble throughout both lung fields which would suggest the existence of a bacterial pneumonia of some type.

The second important point is that this patient was treated with antibiotics without response to heavy antibiotic therapy. This suggests many interesting possibilities such as metabolic derangement, illness, disseminated intravascular coagulation, disease possibly of plasma, or the bacteriologic which is entirely refractory to ordinary therapy such as streptomycin, penicillin, or erythromycin. The absence of sputum or thoracic cultures is unfortunate for the finding that they would be of help. If we were dealing with a pneumococcal pneumonia or a group A beta hemolytic streptococcus.

or *Staphylococcus aureus* or Friedlander's pneumonia we would get a profuse growth on sputum culture. A fungus culture might have been equally helpful.

Terminally the patient developed more rales and severe cyanosis with nasal oxygen the cyanosis disappeared. I don't believe that this was a sign of improvement for cyanosis frequently will disappear in severe pneumonia after consolidation is complete. We also see that the patient became oliguric and that his blood urea nitrogen rose while red blood cells and albumin were found in his urine. Despite all measures he lapsed into coma and developed Cheyne Stokes respiration. Terminally he developed what appears to be pulmonary edema and cardiac failure also quite common in severe pneumonias. It is fair to assume that the patient died with solid lungs and the indications are that he had some type of terminal kidney involvement probably an acute interstitial nephritis or a focal or embolic affair. From the protocol we can conclude that we are dealing with a suddenly developing process in an essentially well young man which has all the features of an overwhelming pneumonia with terminal nephritis and that this process is not stopped or stayed by antibiotics and that the patient goes irrevocably downhill to his death. With such a case almost everything must be considered and I shall try to consider as many possibilities as are reasonable in a brief period of time.

Neoplasm is unlikely because of the fulminating course although an acute leukemia might give a similar picture. But the blood counts are not suggestive. Similarly pulmonary fungus and pulmonary tuberculosis may be discarded because of a too fulminating course, absence of sufficient roentgenographic changes and the presence of marked leukocytosis. Virus pneumonia is equally unlikely to produce such a fulminating course with leukocytosis. The rickettsial diseases could give a clinical picture similar to this one. In their severest forms the onset of these diseases is characterized by malaise, head ache, aches and pains, fever and cough. Usually these diseases show a slow pulse and a high fever but in severe cases the pulse may be as rapid as the temperature is high. Without a body or extremity rash rickettsial disease becomes very unlikely. Further these diseases respond well to the mycin group of antibiotics while the therapeutic effects of the mycins with this patient were quite negligible. We can consider these diseases or at least not rule them out entirely.

Now consider the interesting possibility that there is no infection whatsoever and that this picture represents a metabolic or inflammatory process secondary to a collagen disease. Are the facial rash and hematuria part of systemic lupus erythematosus? Lupus with very marked pleural pulmonary manifestations will give massive pulmonary consolidation with dyspnea, cyanosis, nephritis, abdominal pain and diarrhea. However there is no history of fever, arthralgias or any evidence of panserositis (endocarditis or arthritis). The white blood cell count is very high for lupus although white counts as high

p rt of the p mary disease A roentgenogram of the chest and an electrocardiogram were taken on admission and we shall have the report now

D + Y k There is well defin d per bro chl pneumo : in th right c d ophrenic gle Findings are cons tent with a b o cho pneumonia at the right base Th s a gr nularity of the l ng f elds bilater lly ltho gh no oth infiltrate is s n The finding re definitely bnorm l b t n nspecific

D + R + E1 electrocardiograms were obtained on the patient on three successive days (9, 10 and 11 April 1955). The tracings are basically similar and are characterized by marked sinus tachycardia, low amplitude and poorly delineated T waves over the lateral precordial leads. These changes are slightly more marked on the tracing of 10 April 1955 which is definitely abnormal. The changes are considered non-specific but could be compatible with underlying myocarditis.

D. G. H. I. f. I. ure that most of the electrocardiographic changes are entirely nonspecific and represent a toxic state.

The patient was treated with large doses of penicillin intramuscularly for the first 24 hours he had 10 loose stools. With the relationship between the diarrhea and abdominal pain. The surgeons believed that his abdominal pain was caused primarily by dehydration yet despite hydration and electrolyte replacement the patient deteriorated.

Several other points deserve comment at this time. First, the x-ray findings are minimal and less than one would expect with such a toxic state. Possible explanations are twofold. One is that pneumonia is not the primary cause of the toxic state but rather that it is reflex to some other process such as dehydration and sepsis or nephritis. A second possibility is that there is considerably more involvement in the lungs than the x-ray indicated. Physical examination led to most cases throughout both lung fields which would suggest extensive acute pneumonia of some type.

The second important point is that this patient was treated with  
therapy without response to her pyrexia or other therapy. This  
suggests many interesting possibilities such as metabolic derange-  
ment, congenital deficiency, rickets and disease or  
possible plasma in the bacterial disease which is entirely  
refractory to ordinary therapy such as staphylococcal or Friedlander's  
infection. The blood of purum thrombocytopenia is unfortunate  
for even if not they would be of value. If we were dealing with  
a pneumococcal pneumonia going up Ab to hemolytic streptococcus

L R f Yur k IC USN R d R d l gy  
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formerly a well known disease entity. Patients were said to be extremely toxic and prostrate and I believe the gray white exudate described here could have been a diphtheritic membrane. All the features of diphtheria are similar to this case and the pneumonia which arises can be severe. Nephritis is characteristic; it usually comes early in contrast to the nephritis of scarlatina which comes late. Myocarditis is present and sudden death is frequent. However we do not have throat cultures and cannot establish the diagnosis. The lack of peripheral neurologic lesions further mitigates against the likelihood of diphtheria in this case.

Pneumonia, diarrhea and nephritis apparently suggested the possibility of typhoid fever. The negative agglutination studies, stool cultures and Widal tests rule out this disease satisfactorily. I shall also mention pleural pulmonary tularemia which could give a picture consistent with that in the protocol. Fifty per cent of tularemia pneumonia cases do not have a bubo or primary ulcer. The diagnosis must be made on history and a rising agglutination titer and we have neither. Tularemia should respond beautifully to streptomycin sulfate but there was no response here.

In conclusion I believe this to represent an infectious bacterial pneumonia but I cannot differentiate between the infectious pneumonias on either clinical grounds or from the protocol material. Relying on percentages and my own experience I would favor one of the coccal pneumonias and inasmuch as large doses of penicillin were without effect.

#### Dr Gorsuch's diagnoses

- 1 Staphylococcal pneumonia
- 2 Terminal interstitial nephritis

#### PATHOLOGIC FINDINGS

Dr Cow II: Thank you, Doctor Gorsuch, for your excellent discussion of this case.

At autopsy the body was that of a well-developed and well-nourished adult young male of Mexican descent. There was a slight edema of the left arm and hand and no other pertinent external findings. The findings of interest were confined primarily to the thorax. Each pleural cavity was found to contain about 400 ml of serosanguineous fluid. The serosal surfaces of both parietal and visceral layers were smooth and the fluid contained no fibrin. There were no adhesions. The pericardial cavity contained about 50 ml of clear yellow fluid. Both parietal and visceral pericardial surfaces were smooth and shiny.

The right lung weighed 1,450 grams and the left lung 1,550 grams. They were extremely heavy, wet and solid and there was a nodular feeling over the pleural surfaces and on the cut surface. The surface



of 11 lobes was similar. It was very dark mottled red as if the extensive massive intr alveolar hemorrhage beneath the surface and focally there were small subpleural hemorrhages particularly posteriorly and on the diaphragmatic surfaces. Crepitation was almost completely absent. The cut surface of all lobes showed a total consolidation on which appeared red lobular infiltration. This was associated with what appeared to be considerable intrapulmonary hemorrhage. In addition there was considerable effusion of red bloody fluid from all cut surfaces. A frothy dem fluid was readily expressed from the cut surface of the lung. The tracheobronchial tree contained hemorrhagic purulent material in addition to the frothy fluid. Pulmonary vessels were not remarkable. There was a large soft reddish-brown lymph node at the hilum of each lung but no gross evidence of tumor. Smears and cultures taken from the bronchi and from the lung surface were negative. There was no bacterial formation and certainly nothing to indicate staphylococcal involvement.

The heart weighed 400 grams. The pericardium was smooth and shiny. The surface was brown and fairly firm. The chambers showed dilatation confined primarily to the left and right atricle more pronounced on the right with flattening of the trabecular carneae and the papillary vessels. The endocardium was smooth and glistening throughout. In the right atricle was an adherent post-mortem clot. The valves were normal in appearance and had normal measurements. The coronary arteries showed no evidence of atherosclerotic change. No thrombi were found in the coronary vessels. Section of the interventricular septum and the left ventricular myocardium showed myocardial degeneration but no evidence of infarction.

The kidneys and liver were grossly normal. Angiography of the spleen was performed.

Microscopic sections of the heart belied the macroscopic gross appearance. The myocardial fibers were normal. In many areas there was a transient increase in frequency of the myocardial fibers. The predominant changes present were in the interstitial tissue and usually in the perivascular region and small intramural vessels of small artery and arteriole size. However, a definite and in many areas widespread fibroid degeneration of the collagen particularly prominent in a perivascular distribution. A moderate interstitial edema usually surrounded the elements of fibroid degeneration and with a high phosporic distribution. Occasionally associated with the vessels were structures which were believed represented early atherosclerotic plaques. These changes in the heart muscle were believed to be characteristic of the early phases of the heart muscle myocarditis.

Section of lung showed that many areas fine architectural detail was completely obliterated by a mass of intrapulmonary hemorrhage with massive fresh blood filling the alveolar spaces and obliterating the alveolar architecture. Elsewhere intrapulmonary hemorrhage was not nearly so marked and prominent changes were evident. These included a thickening of the alveolar wall and interstitial tissue.

and in these alveolar walls or in the interstices of the lung in a widespread fashion was a diffuse and prominent infiltrate of fairly large mononuclear cells with an occasional neutrophil. There was pronounced and extreme congestion. The alveolar walls were thickened and the alveolar lining cells were increased in size and frequently cuboidal and macrophage like in appearance. In almost all of the alveoli there was a fibrinoid material that was closely opposed to the alveolar wall and took on a hyaline membrane like appearance such as is seen in a hyaline membrane disease of the newborn or in viral or atypical pneumonia. There was no frank bronchopneumonia. These changes were diffuse and present in all the sections of the lung. Edema fluid also was seen focally in the alveoli.

Sections of the kidney showed normal glomeruli but a moderate cloudy swelling of the tubular epithelium. Mononuclear cells composed a focal cellular infiltrate in the cortical regions. They appeared to be arranged about small arterioles with questionable fibrinoid changes.

#### Pathological Diagnoses

- 1 Acute rheumatic fever with acute massive rheumatic pneumonia bilateral involving all lobes
- 2 Rheumatic myocarditis, acute, and rheumatic arteriolitis, liver and spleen and kidneys
- 3 Intrapulmonary hemorrhage extensive
- 4 Bilateral hydrothorax (400 ml)
- 5 Congestion and edema of the lungs
- 6 Multiple subpleural hemorrhages

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#### DOES FERROUS SULFATE AFFECT THE GUAIAC TEST FOR OCCULT BLOOD?

The blue color of the positive reaction results from the oxidation of a phenolic compound in gum guaiac. This oxidation is possible by hydrogen peroxide if catalyzed by a peroxidase. Hemoglobin has such peroxidase activity and produces the oxidation by hydrogen peroxide giving a deep blue color. Iron does not have such a catalytic power and thus cannot give a positive reaction.

—EDITORIAL

*in Southern Medical Journal*  
p 554 Apr 1957

## Hereditary Spherocytosis in a 41 Year Old Man

JACK BROOK L. *1st Lt MC USNR*  
JOHN B. M. GREGOR *Cpt MC USN*  
THIRL E. JARRETT *Cpt MC USN*

**H**EREDITARY SPHEROCYTOSIS or congenital hemolytic anemia is most frequently diagnosed in children or young adults. Debre and his co-workers reported 90 cases in which the diagnosis was made before the age of 14 years. Occasionally, however, the disease has been diagnosed shortly after birth when a special attempt is made to establish the diagnosis because of the presence of the disorder in one of the parents or a sibling. The diagnosis is seldom made in adults admitted for unrelated complaints unless it has been noted that other members of the family have been affected.

Young Izzo and Platzer<sup>1</sup> in their report of 28 cases noted that symptoms were first detectable at the age of 5 years or younger in 14 of their cases. In 8 the onset of symptoms occurred between the ages of 10 and 40 years and the remaining 6 had no symptoms referable to the disorder. Nine of the 28 cases were the original members of families investigated and a prolonged duration of symptoms (16 to 28 years) was present in only four of these patients. Only one in their series was over 40 years of age when the diagnosis was established.

The following case is presented because of the long duration of recurrent symptoms and the age of the patient (41 years) when the diagnosis was finally established.

### CASE REPORT

A 41-year-old man was admitted to the U. S. Naval Hospital in Philadelphia on 25 November 1957 because of malaise, anorexia, abdominal pain, and weakness of the right arm and left thumb and dark urine for several days duration. History obtained at that time revealed that he had had scleral icterus intermittently since 1942 and of infectious mononucleosis with jaundice in 1942. The physical examination was entirely negative except for mild scleral icterus and an abnormally enlarged spleen.

From the Naval Hospital, Bethesda, Md. L. Brook was a USN 1st Lt. P. M. Gregor and T. E. Jarrett were USN 1st Lt.

Laboratory examinations revealed a hemoglobin of 9.3 grams per 100 ml hematocrit 28 ml per 100 ml red blood cell count 2 900 000 per  $\mu$ l white blood cell count 6 500 with a normal differential count. Peripheral smear showed moderate anisocytosis marked hypochromia and a few polychromatophilic red cells. The mean corpuscular volume was 97 mean corpuscular hemoglobin 32 mean corpuscular hemoglobin concentration 30 and reticulocyte count 2.3 per cent. Erythrocyte osmotic fragility test was normal. The Coombs test was negative. Urinalysis and serologic tests for syphilis were negative. Serum bilirubin was 3.04 mg per 100 ml (direct 0.50 mg indirect 2.54 mg) cephalin cholesterol flocculation was 3 plus in 24 hours and 48 hours and thymol turbidity was 3.4 units.

In view of the intermittent icterus and persistence of slight scleral icterus the patient was transferred to this hospital on 17 December 1957 to rule out a familial type of hemolytic anemia.

The patient was of Prussian descent. His mother and two siblings were living and well but no information was available about his father who had deserted the family when the patient was 6 years of age. The maternal grandparents had died in their eighties. His father's brothers were living and well. No family history of anemia jaundice hemorrhage or gall bladder disease was obtained. His wife—of Irish descent—and five children were living and well.

The patient stated that as a child he had had frequent nose bleeds requiring cauterization on one occasion. He denied ever having had leg ulcers intolerance to fried or fatty food or gallbladder disease. On reviewing his past history at this time the patient stated that his first episode of scleral icterus dark urine malaise abdominal pain anorexia irritability and a distaste for smoking occurred in March 1942 while aboard a ship at sea. Treatment consisted of bed rest and a low fat diet and he recovered in three weeks. In June 1942 he had a recurrence of symptoms and was hospitalized at the U S Marine Hospital Cleveland Ohio because of icterus and left upper quadrant tenderness. Laboratory examinations at that time revealed an icteric index of 30 a normochromic normocytic anemia and a slightly increased red cell fragility and two weeks after admission the peripheral count showed an increase in the number of lymphocytes (of which a moderate number were atypical) a reticulocyte count of 14 per cent and the heterophile agglutination was positive in 1:1024 dilution. His diagnosis at this time was believed to be infectious mononucleosis with splenitis and jaundice.

The patient stated that since 1942 he had noted a recurrence of his symptoms each year either in the spring or fall. Each attack was rather mild except for the one requiring hospitalization in 1942 and the present episode. During recurrence of symptoms he was able to perform his duties provided he had a good deal of bed rest a low fat diet and plenty of fluids. These attacks would last about three or four weeks were unaccompanied by fever and would subside.

spontaneously. The present episode was preceded by an upper respiratory infection but no history of infection preceding previous attacks was established. Neurologic symptoms namely numbness of the right arm and left thumb were only associated with the present attack.

Physical examination on admission to the hospital 17 December revealed a well nourished well developed white man with slight cretinitis of his palms and metacarpal spaces and minimal sclerotic keratosis. The liver was not palpable. Traub space was dull to percussion and the splenic tip was thought to be palpable. He stated that his urine was becoming lighter in color. The remainder of the physical examination was within normal limits.

Laboratory studies on admission revealed the following: hemoglobin 13.9 gms per 100 ml, hematocrit 41 ml per 100 ml, red blood cell count 4,450,000 per  $\mu$ l, white blood cell count 11,500 per  $\mu$ l with a mild differential: neutrophils 50 percent, and platelets 110,000. The peripheral smear revealed hypochromic normocytic red cells, a moderate number of metachromatic granules, some basophilic and polychromatophilic cells (fig. 1). The blood urea nitrogen, fasting blood sugar, total protein, albumin, globulin, alkaline phosphatase, electrolyte determination, rate of coagulation, heterophilic cold agglutinin, and urinalysis were negative.

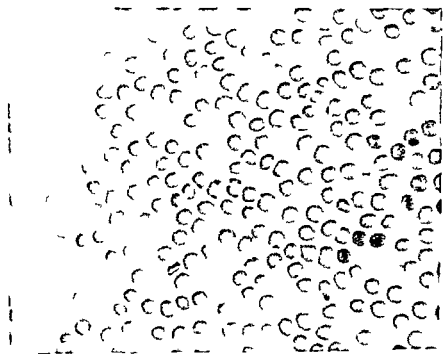


Fig. 1. Peripheral smear showing typical metachromatic granules. ( $\times 430$ )

The serum bilirubin was 3.0 mg per 100 ml (direct 0.13 indirect 2.87). Cephalin cholesterol flocculation, prothrombin time and thymol turbidity were negative or normal. There was no bile in the urine and the urinary urobilinogen was 0.55 mg per 100 ml. A 24 hour urine was collected and the coproporphyrin level was 7.43  $\mu$ g per cent (normal 50 to 300) and the uroporphyrin level was 1.66  $\mu$ g per cent (normally up to 0.5). After one week the coproporphyrin and uroporphyrin levels became normal. The serum bilirubin gradually decreased in the indirect fraction.

A red cell osmotic fragility test was performed and hemolysis with the patient's blood began at 0.48 and was complete at 0.36 with the control's blood it began at 0.44 and was complete at 0.32. An incubated red cell osmotic fragility test was then performed and hemolysis began at 0.68 and was complete at 0.44 with the patient's blood while with the control's blood it began at 0.56 and was complete at 0.40. The latter test was repeated one week later and with the patient's blood hemolysis began at 0.85 and was complete at 0.40 and with the control's blood hemolysis began at 0.68 and was complete at 0.28.

A bone marrow aspiration showed erythroid hyperplasia. Hemoglobin electrophoresis revealed hemoglobin A and the alkali denaturation was normal. Serum electrophoresis showed a moderate decrease in the alpha 2 fraction, a minimal decrease in the beta fraction and was otherwise normal.

In the erythrokinetic study the plasma iron disappearance half time was 22 minutes (normal is from 60 to 120 minutes), the plasma iron turnover was 3.59 mg per kilogram per day and the red cell survival half time was 14 days (normal is from 25 to 35 days). The impression gained by this study was that of an accelerated  $\text{Fe}^{59}$  removal from the blood stream but the overall turnover was normal. In vivo counting revealed an ascending curve for  $\text{Fe}^{59}$  in the spleen which may indicate hypersplenism.

Roentgenographic examinations of the chest, skull and long bones were within normal limits. A gallbladder series showed a normally functioning gallbladder with no calculi.

The above findings confirmed the diagnosis of hereditary spherocytosis despite the age of the patient, his age at the onset of symptoms and the doubtful splenic enlargement. This diagnosis was further substantiated after examination of the patient's wife and five children. The oldest son, age 14 years, who had been asymptomatic, revealed typical spherocytes in moderate number on peripheral smear. His hemoglobin was 14.7 grams per 100 ml and the reticulocyte count was 2.4 per cent. No splenomegaly, however, was detected. The next oldest child, age 13 years, also showed typical spherocytes in moderate number on peripheral smear, hemoglobin 13.2 grams per 100 ml and reticulocyte count was 3.2 per cent. On examination of his abdomen, Traube's space was dull on percussion and the splenic tip was palpable. The incubated osmotic fragility test showed that hemolysis

began at 0 80 and was complete at 0 32 f b th of these children while h molysis of the c tr l blood began t 0 68 and w complet at 0 24 The wife d em g ch l d n were found to be norm l

On 13 February 1958 a sple ct my wa perfo med At operat on the pl n was noted t b greatly enl rg d me suri g 19 by 12 5 by 9 cm i ts greatest diam te a d we gh: g 852 gr m In ddition an access ry spleen me suri g 2 by 1 by 0 6 cm wa removed from the s len en l l g ment Smears made from the splenic pulp at the time of surgical i terv nt on showed 50 per cent spher cyt s M c o s c o p i c x a m i n a t i o n of the spleen was compatible th c ent l hemolytic anemi Post pe at vely the plat let count r se gr d lly to 800 000 per  $\mu$ l by th nd of the f st we k a d th d cr a d to normal l ls where p p r t vely a thr mbocytopen a of 90 000 w ted Two weeks post p r t vely th p ph l smen re ale d 20 to 30 p r cent spherocyt d How ll Jolly b dies An incub t d osmotic f g l ty study w p t d at th s t m nd the h m l y began at 0 76 and was compl t t 0 44 w th the pat t s bl d h moly i w th the co tr l blood began at 0 56 nd w s complete t 0 36

The pat ent m de n v n t f l recovery from plenectomy nd w di chrg d from the h pit l H and h s two children who h r e the d ord r to be examined p r o d lly

#### COMMENTS

The presence of recurrent episodes of jaundice malaise weakness and spherocytes on peripheral smear in a patient over 40 years of age may well indicate a diagnosis of hereditary spherocytosis The presence of spherocytosis and increased osmotic fragility especially after incubation however may be found in other hemolytic disorders during periods of very rapid hemolysis but the persistence of abnormalities even after splenectomy is an important characteristic of hereditary spherocytosis In addition the spleen is almost always enlarged although in some cases it cannot be palpated Therefore the absence of splenomegaly should not preclude a diagnosis of hereditary spherocytosis The unequivocal diagnosis of hereditary spherocytosis should be made only when spherocytes are demonstrated in the patient and in one or more relatives as in this case

The studies of Race and Meulengracht indicate that hereditary spherocytosis is probably inherited as a Mendelian dominant Little was known of the patient's family background of illnesses but the diagnosis of hereditary spherocytosis was confirmed in two of his five children It is interesting to note that only two of his five children had this disorder Family studies of Race Young Izzo and Platzer and Young also demonstrated a shortage of affected offspring of a propositus (less than the expected 50 per cent incidence)

We wish to re-emphasize that in an older patient with spherocytes in a peripheral smear, a questionably enlarged spleen and a supposedly negative family history, the possibility of hereditary spherocytosis should not be eliminated until the entire family has been investigated.

### SUMMARY

A case of hereditary spherocytosis is presented in which the diagnosis was made when the patient was 41 years of age and had had annual recurrence of symptoms for the past 16 years. Enlargement of the spleen was doubtful on physical examination, but at operation it was found to be greatly enlarged. The unequivocal diagnosis of hereditary spherocytosis was made by investigating the family and finding the disorder present in two of the patient's children. Splenectomy caused no change in the spherocytosis or the red cell osmotic fragility, as has been previously reported by other investigators in confirmed cases of hereditary spherocytosis.

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# Necrobiosis Lipoidica Diabeticorum

VIRGIL H VOSS *Capt USAF (MC)*

**E**VERY physician should be familiar with the more common skin manifestations of diabetes mellitus. Genital or rectal pruritus, submammary intertrigo, and pyogenic or monilial infections are among the skin conditions requiring exclusion of this disease. In a recent issue of the *Journal* a relatively rare skin condition associated with diabetes, xanthoma diabeticorum, was described. An even more unusual and much more recently described skin lesion usually associated with diabetes mellitus is necrobiosis lipoidica diabeticorum. In the case herein described this uncommon skin condition proved to be the harbinger of the systemic disease.

The entity necrobiosis lipoidica diabeticorum was described by Oppenheim in 1929 and in 1939. He named the condition dermatitis atrophicans lipoides diabetica. Urbach described a similar case in 1932 and gave the condition its present name.

## CASE REPORT

The patient, a 30-year-old Caucasian, was first seen during military sick call. His chief complaint was persistent pruritic areas of skin eruption on the lower legs extending from the ankles to the knee joint. He stated that it was approximately two years since the first lesions appeared and that he had seen several physicians in the interim who had prescribed various ointments and lotions to no avail. Because the lesions caused the patient difficulty other than the cosmetic blemish he did not become too concerned about them.

In the course of our yearly system review the patient mentioned that he had lost about 35 pounds in the previous 12 months despite the fact that his appetite had increased. The patient also volunteered the information that he seemed to be drinking more fluids in recent months and that he had concomitant polyuria.

The patient was hospitalized following a urinary tract infection which required a 4-day glycosuria. After further study he was treated for diabetes mellitus. His present history was negative for other significant illnesses. He had been hospitalized in the U.S. Air Force hospital for the removal of a neuroma from the dorsum of his right hand about 13 months

prior to his present hospitalization. A check of the results of the laboratory work performed at that time revealed that the preoperative urinalysis had been reported as "normal."

Family history was negative for diabetes insofar as the patient knew. He was familiar, however, only with the paternal side of his lineage.

Physical examination did not show any evidence of marked recent weight loss, though the patient was somewhat asthenic in appearance. A comparison of his appearance on admission with a photograph taken a year before, however, substantiated his statement of marked weight loss (fig. 1 A and B). On the lower extremities were numerous plaque-like areas, varying in size from 1 cm in diameter to a confluent

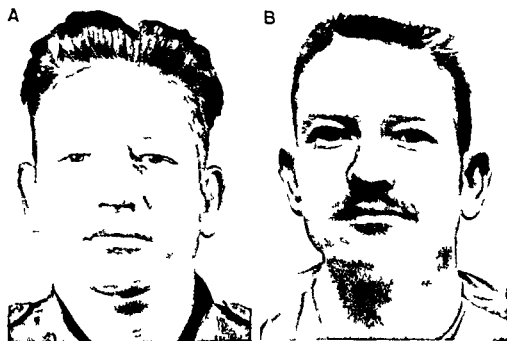


Fig. 1. Appearance of patient (A) 12 months prior to his hospitalization; (B) on admission to the hospital.

area involving the lateral malleoli of both ankles (fig. 2 A and B). The smaller lesions were of violaceous hue, while the larger varied in color from a dark red to a yellowish brown. Slight evidence of scaling was seen on the surface of some of the lesions. Their surface were cartilaginous to touch and were nontender to pressure. Physical findings including fundoscopic examination were otherwise negative.

A routine roentgenogram of the chest revealed no significant abnormality; a flat plate of the abdomen did not show any evidence of calcification of the pancreas, and roentgenograms of the joints were negative for evidence of blood vessel calcification.

Significant laboratory studies revealed blood glucose (fasting) of 380 mg per 100 ml a total serum cholesterol of 164 mg per 100 ml (38 per cent as esters) and normal complete blood cell count. Urinary was negative except for a 4 plus urine.



Figure 1. Photograph of patient's legs (A) taken from the right and (B) taken from the left demonstrating the symmetrical deformities.

Details of this patient's hospital course are pertinent to the purpose of this article. Management of his diabetes was brought about by gradually increasing doses of insulin. He had a random 2200-ciloride betacel test. At the time of his discharge from the hospital he was taking 40 units of ultrapotassium Hagedorn units and 15 units of ultralinsulin each morning.

### DISCUSSION

Unfortunately, the patient was transferred before a pathologic confirmation of the clinical impression of necrobiosis lipoidica diabetorum was obtained, but a review of the literature revealed that it has not been uncommon to report cases without microscopic confirmation. A survey of the literature from 1919 through 1940 shows that of 54 cases described only 3 included histologic descriptions. Hildebrand, Montgomery, and Ryngaert

stated. It should be possible to make a diagnosis of necrobiosis lipoidica diabetorum on the clinical appearance of the lesions alone." Rattner<sup>6</sup> confirms the fact that the lesions of this condition are typical clinically—in fact, even more so clinically than histologically.

Microscopically, the lesions are variously described in the literature, the most consistent features being a normal or slight atrophy of the epidermis, a dilatation of the capillaries of the superficial layers of the cutis, and a degenerative or "altered" appearance of the connective tissue in the cutis.<sup>7</sup> Elastic tissue is lost. Lipoids are observed in the region of the degenerated collagen fibers, and these characteristically stain a reddish brown with sudan III.<sup>7</sup>

An excellent summary of the gross features of the lesions of necrobiosis lipoidica diabetorum were presented by Hitch.<sup>8</sup> The typical lesion may go through four phases: (1) a small reddish, infiltrated papule; (2) an increasingly larger lesion which takes on a violaceous hue; (3) a slightly raised, firm, yellow plaque which may soften and sometimes ulcerate; and (4) a flattened, yellowish region with central atrophy and depression, and a peripheral irregular scaling red region of infiltration. In a patient with necrobiosis lipoidica diabetorum, lesions may be found demonstrating any one or a number of these phases.<sup>9</sup>

The lesions are usually bilateral, and are most often found on the lower extremities. Almost any other area of the body may be involved, however. About 90 per cent of the cases described are in women. The first cases cited in the literature were invariably associated with diabetes mellitus, but subsequently a number of cases of necrobiosis lipoidica diabetorum have been reported in which no concomitant diabetes could be detected.<sup>9, 10</sup>

Incidence of the condition is variously estimated. An estimate of one case of necrobiosis lipoidica diabetorum in 1,000 diabetics is made by one author.<sup>11</sup>

The pathogenesis of necrobiosis lipoidica diabetorum remains obscure. Trauma, hyperglycemia, hyperlipemia, insulin circulatory disturbances, diet, and a number of other factors have been implicated without substantiating proof.

No effective treatment has been found. Regulation of diabetes, subcutaneous injection of insulin beneath the lesions, and roentgen or ultraviolet therapy have not proved significantly effective.<sup>12</sup> The lesions are usually asymptomatic, however, and sometimes they resolve spontaneously.

#### SUMMARY

A case of previously undetected diabetes mellitus in a young white male whose chief complaint was a peculiar "skin

eruption involving his lower extremities is described. On the basis of the characteristic appearance and location of the skin lesions in association with diabetes a diagnosis of necro lipoidica diabeticorum was made. A brief discussion of this condition is presented. An awareness of this rather unusual dermatologic manifestation of diabetes should be fixed in every physician's mind because it may serve as a guide to the detection of the more significant systemic disease.

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## OVERCONSCIENTIOUS ANONYMITY

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—RICHARD ASHER M. D.  
*Brit. h. M. d. l. J. m. l.*  
 p. 503 23 A. g. 1958

# Neurological Symptoms Possibly Related to Poliomyelitis Immunization

EDWARD S. MORGAN *Captain MC USA*

**N**EUROLOGICAL complications of immunization procedures sometimes occur in vaccination for smallpox,<sup>1</sup> pertussis,<sup>2</sup> typhoid,<sup>3</sup> and rabies.<sup>4</sup> Since 1954 the Salk vaccine for immunization against poliomyelitis has been widely used in this country. The following is a case report of a patient who developed neurological symptoms soon after immunization with Salk vaccine.

## CASE REPORT

The patient, a 25 year-old white nurse, was admitted to this hospital on 24 April 1957. Two days prior to admission she noted weakness in her right leg. The next morning she awoke with a moderate frontal headache, generalized malaise and weakness and pain in the lumbar area, the right gluteal area and in the right leg. Her temperature was 101°F. She put herself on Terramycin (brand of oxytetracycline) 250 mg four times a day and inasmuch as she was off duty, spent the day in bed. On the day of admission her symptoms persisted and in addition she noted pain and weakness in her right arm. She was admitted to the communicable disease service of this hospital as a possible case of poliomyelitis.

The past history revealed a fracture of the left ulna in 1952, an appendectomy in 1953 and a dilatation and curettage for functional bleeding in 1956. There was no history of allergy in the patient or in her family. The father had died at age 32 as a result of heart disease and pneumonia. Her mother and one sister were alive and well. The patient had received no injections in the previous six months except for her first poliomyelitis immunization with the Salk vaccine in her right arm on 13 March, six weeks before admission, and her second poliomyelitis immunization in her left arm on 22 April, about three hours before she became ill.

Physical examination revealed an acutely ill young woman. Her oral temperature was 99.9°F, respirations 22 per minute and normal in depth, pulse rate 106 per minute and regular, and her blood pressure

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From William B. Um, Army Hospital, El Paso, Texas. Dr. Morgan now in the Department of Medicine, University Medical Center, Stricker Memorial Hospital, 260 Cottage Blvd., Rochester, New York.

was 170/75 mm Hg. Her pharynx was mildly injected but there was no subjective soreness. Funduscopic examination of the eyes was normal. There was mild weakness of the patient's right arm and leg but no muscle atrophy was noted. All sensory modalities and cranial nerve were normal. The deep and superficial reflexes were active and equal.

Laboratory examination revealed a white blood cell count of 10,200 per  $\mu$ l with 62 per cent neutrophils, 32 per cent lymphocytes, 2 per cent monocytes and 4 per cent eosinophils. Urinary and serologic test for syphilis were negative. The hemoglobin was 14 gm per 100 ml and hematocrit was 39 ml per 100 ml. Roentgenographic findings of the chest, pelvis and lumbosacral spine were normal. A lumbar puncture on admission revealed a clear colorless fluid with a protein of 110 mg per 100 ml and a closing pressure of 80 mm of water. No blood cells were found. The spinal fluid sugar was 75 mg per 100 ml, the chloride was 100.5 mEq per liter and the total protein was 66 mg per 100 ml. The spinal fluid was sterile and culture were negative. The electroencephalograph was normal. A culture of material from the throat was negative. The heterophil to total was 1/7 and no atypical lymphocytes were found.

The patient was placed on absolute bed rest, heat and cold was placed over her legs and codeine was administered as needed for 48 hours for relief of pain. Morphine and spasm gradually subsided in 72 hours but muscle weakness became more marked. For the first 20 hospital days the patient had a temperature above 99.5 F. At this time part of each day. No localizing test for infection could be found. After the twentieth day she became afebrile and remained so for the rest of her hospitalization. Her deep tendon reflexes and sensation were normal at all times. An ophthalmologist found no fundus, extraocular muscles and visual fields to be normal. A physiotherapist confirmed the muscle weakness of the right proximal lower extremity and started physical therapy to the right thigh and distal reeducation of the affected muscles. Neurological and neurosurgical consultants believed that the patient did not have poliomyelitis but was unable to make a final decision. Clinical course.

By the sixth hospital day the patient began to have rapid recovery of muscle strength. By the eighth hospital day she had regained normal muscle power in her right arm but the right leg was still weak. She was ambulatory but although she had no pain her gait was markedly abnormal. A repeat lumbar puncture on the third day revealed clear colorless fluid with normal dynamics and pressure. The spinal fluid sugar was 60 mg per 100 ml, the chloride was 128 mEq per liter and the total protein was 62 mg per 100 ml. Again no blood cells were found and the culture was negative.

The patient continued to improve on physiotherapy. On the twenty-fifth hospital day a repeat lumbar puncture revealed clear colorless fluid with pressure of 80 mm of water. No blood cells were found and the culture was negative. The spinal fluid sugar was 65 mg per 100 ml.

the chloride was 125 mEq per liter and the total protein was 36 mg per 100 ml. By the forty fifth hospital day the patient's gait was normal. There still was slight weakness of her right gluteal muscles. She was shown how to do the physiotherapy exercises at home and a 30 day convalescent leave was granted.

On 5 July the patient returned from leave with only a trace of muscle weakness in her right leg. She was therefore returned to duty on 8 July. On re-examination in October she had no discernible muscle weakness at all.

### DISCUSSION

The aim of prophylactic immunization is to stimulate the formation of protective antibodies by exposing the host to an antigen. A small percentage of patients immunized against small pox, pertussis, typhoid fever, and rabies develop neurological complications after immunization. The pathologic picture in fatal cases is described as primarily one of myelin destruction, perivascular lymphocytic infiltration, and microglial proliferation with little damage to the nerve cell.<sup>5</sup> Although the pathophysiology of such complications is unknown, the most accepted theory today is that these neurological sequelae may be related to antigen-antibody reactions that take place in nervous tissue.<sup>6</sup> Inasmuch as these complications have been observed following widespread immunization involving the parenteral use of biologic materials, the possibility exists that neurological symptoms might develop in some patients receiving Salk vaccine.

A precise diagnosis of this patient's illness was not made. Poliomyelitis seems unlikely because there was never any stiffness of the neck or any associated neurological signs; no blood cells were present in the spinal fluid even in the active stage of the illness when muscle weakness was progressing, and the patient continued to run a low grade fever without a site of infection for the first 20 hospital days even while clinically regaining muscle strength. It seems more tenable to postulate that she developed an ill-defined neurological illness following poliomyelitis immunization. The temporal relationships of the first and second injections of Salk vaccine and the appearance of the neurological symptoms in this patient fit the current concept of the allergic nature of such sequelae. Sufficient time elapsed after the first injection to permit formation of antibodies which could then react promptly with the antigen introduced in the second injection to cause symptoms.

The occurrence of neurological symptoms after immunization with the Salk vaccine has been mentioned by Nathanson. Since the U. S. Public Health Service is interested in receiving reports of all suspicious cases, a summary of this case was forwarded to Dr. Nathanson. While it was certainly not proved that this patient's illness was related to the Salk vaccine, the possibility of such a relationship is suggested. Since the neurological



complications of vaccinations are so rare it is only by reporting all suspicious cases that it will be established whether or not they may follow immunization with the Salk vaccine

## SUMMARY

A patient with a neurological disease following immunization for poliomyelitis with the Salk vaccine is presented. The possibility that this illness might be a neurological complication of the immunization procedure is discussed.

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## GOOD MANNERS IN MEDICAL WRITING

Readers entitled to expect ducated writ g fr m medical auth r m mbers of wh t Osler called in the l ngu g of his d y th p o f e s s i of a culti ted g ntle- m They re e t t l d to e p e c t th t facts and ideas will be cle r n a writ r m n d b e f r h commits them to p p e and th t h w l l t y t e p e s them in th best d m o t p p r o p r a t e word Th s i j t a m t t e r f good manners but s Sir Arthur Quiller-Couch has s id Style n w r t t g m ch th m th g g o o d m n n r s in other h m n t c u s W m t c o n s i d e r the re d d p t o r l i h i p l c f w e r e to c o m m n i c t e w th him eff t l y & h a l l the th a t it r a t h r che p t o f f him u n l b l e d t a o m u d d l d d e a th t t s p r e m p t u o u s to x p c t him t d s t n d r p e r s n l j a g o w d n d p h r s e s n d o u n o r t h d b b e i t o n s th t t s o f f e n e to o n f n t him w i t h c u d i t e s f e x p r s i n n d the m b g u i t i e i n s e p r b l f r m f l y g r a m m n d s e n t e c e o n s t r c t o n

— *The M. d. J. m. l. J. A. t. l.*  
p 131 J ly 26 1958

## GEN NIESS NAMED CHIEF OF AIR FORCE MEDICAL SERVICE TO SUCCEED GEN OGLE

Major General Dan C Ogle Surgeon General of the Air Force for the past four years who retires on 30 November after almost thirty years active service will be succeeded by Major General Oliver K Niess since September 1954 Command Surgeon of the Pacific Air Forces with headquarters at Hickam Air Force Base T H

A chief flight surgeon since 1932 General Ogle has dedicated himself to aeromedicine in its broadest aspects Under his administration the Air Force has realized its goal for an Aeromedical Research Center at Brooks Air Force Base Texas and the construction of 170 new medical facilities world wide He has brought the level of Air Force military medicine to a new high through his active participation in medical hospital and scientific organizations



*Gen al Ogle*

A native of Keithsburg Illinois General Ogle received his medical degree from the University of Illinois College of Medicine in 1929 and entered the U S Army Medical Corps as a first lieutenant In March 1942 as surgeon of the Technical Training Center in Miami Beach Florida he organized the medical service within the Miami area and developed a 3 000-bed hospital center including a regional hospital in Coral Gables In December 1944 he was assigned as surgeon of the Fifteenth Air Force in Italy where he pioneered the development of a medical service to support strategic Air Force operations The following year he returned to the United States where he became Surgeon of Air University and instructor in medical subjects

Upon graduating from the Air War College in June 1949 General Ogle was assigned as Special Assistant to the Surgeon General and subsequently as Deputy Surgeon General One of the few senior Air Force Medical Service officers who had commanded a general hospital

# GEN DECOURSEY RECEIVES SECOND STAR WERGELAND AND CRAWFORD PROMOTED

A brigadier general and two colonels of the Army Medical Service were promoted in mid-October in widely separated ceremonies held in Texas, France, and Washington.

At Fort Sam Houston, Texas, Brigadier General Elbert DeCoursey, commandant of the Army Medical Service School, received the two stars of major general from Lieutenant General Guy S. M. Loy, commanding officer of the Fourth United States Army. General DeCoursey assumed his present position at Brooke Army Medical Center in 1955 after having served as Director of the Armed Forces Institute of Pathology in Washington. He is a graduate of the University of Kentucky and Johns Hopkins University School of Medicine.

Colonel Floyd L. Wergeland, Executive Director, Office for Dependents Medical Care, was promoted to brigadier general in



Brigadier General Floyd L. Wergeland, MC USA, receives star from Major General Guy S. M. Loy and Major General Floyd L. Wergeland, J. MC USA, with his family.

Ceremony held in the office of Major General James P. Cooney, Deputy Surgeon General of the Army. General Wergeland was chief of the personnel division in the Office of the Army Surgeon General from February 1957 to the reorganization of May of this year when he

was made Assistant to the Executive Director for the Medicare program. He became executive director of the program in September. He received his medical degree from the College of Medical Evangelists in 1972 and is a 1954 graduate of the National War College.



Mrs. John L. Crawford pins on her husband's new stars in Orleans France with daughter Marie looking on.

Colonel John L. Crawford, Commanding Officer of the 9th Hospital Center Landsuhl Germany, was recently promoted in a ceremony at Headquarters U S Army Communications Zone Europe Coligny Caserne Orleans France. Prior to his assignment as commanding officer 9th Hospital Center, he was the Surgeon, United States Continental Army Command Ft Monroe Virginia from 1953 to 1959. He is a 1937 graduate of the Indiana University School of Medicine.

### Coming Meetings

Association of Military Surgeons of the United States, Statler Hotel, Washington D C 17-19 November 1959

National Conference on Air Pollution, Sponsored by the United States Public Health Service, Sheraton Park Hotel, Washington 18-20 November 1959

## A MESSAGE FROM THE A M A

Recently there has been a renewed interest in proposals for the utilization of the experience and talents of military reservists in civil defense. There is little doubt that the present civil defense organization requires reinforcement and strengthening, if it is to meet the demands of an enemy attack or other large scale natural disaster.

At the annual convention of the Reserve Officer Association in June 1958 a resolution was approved in which it was proposed that the Reserve Officers Association and the National Guard Association in co-operation with the Department of Defense and the Office of Civil and Defense Mobilization make a joint study of ways and means to employ the skills and experiences of standby active and retired reserve officers of the reserve component in formulating a practical plan for civil defense.

Then on 19 August 1958 Senator Carl T. Curtis of Nebraska recommended on the floor of the Senate that the nation utilize military reservists in civil defense work. Senator Curtis pointed out that the job of civil defense is so great that if it ever becomes necessary to perform it additional help will be required. At such time disciplined units that know what to do and have the ability to do it would be of inestimable value.

Senator Curtis suggested that reservists of all military branches should be unified and assigned the major responsibility for civil defense. Such reservists could earn participation and retirement credits by teaching or attending classes with nonreservist civil defense workers and the general public. Lectures and exercises on the civil defense problems of individual survival methods, water and food supply, public health and sanitation, police methods, first aid and medicine, transportation, communications, engineering and other matters would prepare the people of the nation to meet a major disaster.

It is natural that the medical profession is concerned with this problem from the viewpoint of the medical and health needs of the civilian population under disaster conditions. Physicians and paramedical personnel must prepare themselves for the management and care of mass casualties that would result from an atomic, biological or chemical attack. Moreover it is incumbent upon the medical profession to exert forceful and dynamic leadership in the civil defense program at national, state and local levels.

In 1956 the American Medical Association upon recommendation of its Council on National Defense approved a resolution

From the Council on National Defense to the American Medical Association  
—Editor

the Surgeon General, U S Army, be requested to permit action in the use of the 200-bed civil defense emergency hospital, and that such instructional activity be made a part of the training programs of reserve units and incorporated as a part of the Department of the Army medical training program for which annual unit training and armory drill pay is permitted. Subsequently, this resolution was extended to include the U S Navy and U S Air Force. This activity was incorporated in the military programs as one step toward the assumption by reserve medical forces medical units of a role in civil defense operations. The excellent work of the Army Medical Service in the conduct of courses on the management of mass casualties at the Walter Reed Army Medical Center and the Brooke Army Medical Center is another most worthwhile activity in this direction. Much more remains to be done.

Reserve medical units of the armed forces are organizations being which are capable of giving the type of service that could reinforce and strengthen the civil defense effort during the initial phases of a disaster situation without dislocating the defensive capabilities of the country. It is a current concept that reserve medical units will not be called and deployed immediately after an enemy attack. Thus, in the interim between the attack and call up and deployment, the services of skilled medical and paramedical reservists could be used to advantage in civil defense work. Moreover, trained reserve medical units would give direction and stability to the work of civil defense medical operations. Additional civilian workers could be more rapidly trained to assume civil defense duties by working with the armed forces reserve medical units. In this way, in a disaster situation, trained civilians could take over civil defense duties more rapidly so that the reserve medical units could be relieved of their civil defense mission and deployed for military duty.

It is noteworthy that the Canadian army is currently training and planning to use its reserve forces as a supplement to civil defense of their country. Canadian experience indicates that there is complete agreement between the army, the reserve units, the civilian medical profession and civil defense officials. This has proved to be a valuable working arrangement.

In conclusion, it may be said that a plan should be developed whereby reserve medical units and individuals, who would not be involved immediately in military operations, should be used to supplement civil defense operations, so that needless suffering and death can be avoided in the event of enemy attack or in any other disaster situation. In addition, as soon as possible, civilians without any military obligation should be trained to fill the positions occupied by medical reservists serving with civil defense so that reserve medical units may be redeployed for military duty.

## GEN McNINCH HEADS ARMY MEDICAL R&D

Lt Gen Emerson L Cummings, Commanding General U S Army Japan (left), Cpt Walworth F Williams, USA and Brig Ge Joseph H McNinch, MC USA, review an honor guard at Camp Zama, Japan, prior to Gen McNinch's departure recently for Washington, D C. The former surgeon of the U S Army in Japan has been named the first commanding general of the new Army Medical Research & Development Command. The headquarters of the new command was formed from the former research and development division in the Office of the Surgeon General.



New Hospital at MATS Hq. This five-story, 250-bed air-conditioned hospital of reinforced concrete was officially dedicated in a ceremony at Scott Air Force Base, Illinois, on 9 November. Colonel Carl B. Stilson, USAF (MC), is the commandant.

## Navy Lecture Series Begins

Kenneth B Babcock M D Director of the Joint Commission on Accreditation of Hospitals was the first speaker of the fourth annual guest lecture series at the U S Naval School of Hospital Administration Bethesda Maryland on 17 October His subject was Hospital Standards as Means of Improvement of Patient Care The other guest lecturers of the series are John P Hagen Ph D Director Project Vanguard U S Naval Research Laboratory 21 November Edwin L Crosby M D Director American Hospital Association Chicago 16 January 1959 George W Latimer Associate Judge United States Court of Military Appeals Washington D C 20 February 1959 and James A Hamilton Professor and Director Course in Hospital Administration University of Minnesota 20 March 1959

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MSTS Plot s Capt F D ( Spike ) Lovejoy MC USN Director of Medical Services Military Sea Transportation Service North Pacific Subarea kneels before Captain Kidd of the Seattle Seafair pirates to receive his honorary degree of pirate Captain Lovejoy along with eight other officers of equal rank received his degree during ceremonies held recently for the departure of the U S S *General A E Anderson* from Seattle



## Professional Courses for Army Officers

A new series of postgraduate professional short courses for Army Medical Service officers will be held in Washington D C at Walter Reed Army Medical Center and the Armed Forces Institute of Pathology and at Brooke Army Medical Center San Antonio Texas Interested officers who are eligible to attend should apply through channels to the Surgeon General Department of the Army Washington 25 D C Attention MEDCOM OF The dates and subjects are

Walter Reed Army Medical Center oral surgery 5-9 Jan surgical nursing 12-17 Jan radioisotopes in medicine 12 Jan 10 Apr institute for personnel officers 9-13 Feb refresher course for laboratory officers 9-14 Feb experimental basis of psychiatric theory 9 Feb 6 Mar management of mess casualties 16-21 Feb institute for comptrollers 16-20 Feb nursing in the medical management of major casualties 9-14 Mar and medical-military application course for nuclear medical officers 23 Mar 24 Apr 1959

Brooke Army Medical Center physical therapy institute 9-11 Feb management of mass casualties 9-13 Feb institute for supply officer 2-6 Mar and surgery in acute trauma 9-13 Mar 1959

Armed Forces Institute of Pathology ophthalmic pathology 9-13 Mar and pathology of the oral region 23-27 Mar 1959

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## DEATHS

KIRNER Stephen Harpe Lieutenant junior grade MSC USNR 1861-1930  
 born 12 May 1902 at New York City New York  
 graduated 1922 from Hamilton College New York  
 from Cornell University Ithaca New York 1926  
 graduated 28 February 1927 from Cornell University  
 September 1928 graduated 27 May 1928 from Cornell University  
 automobile accident

MALDONADO-RIVERA Miguel Angel Captain USAFR (MC) 1861-1930  
 born 12 May 1902 at New York City New York  
 from Brooklyn graduated 1922 from Cornell University  
 School of Medicine graduated 1926 from Cornell University  
 from Cornell University 6 August 1926  
 died 26 August 1928 at Fort E. W. Carr Air Force Base  
 gun hit while und

STANSON E. B. Captain USAF (MC) 1861-1930  
 born 12 May 1902 at New York City New York  
 graduated 1922 from Cornell University  
 from Cornell University 6 August 1926  
 died 26 August 1928 at Fort E. W. Carr Air Force Base  
 gun hit while und

## Reviews of Recent Books

**COLD INJURY GROUND TYPE** Medical Department United States Army in World War II by Colonel Tom F. Whayne MC USA (Ret.) and Michael E. DeBakey M.D. Prepared under the direction of Major General S. B. Hays MC USA Editor in Chief Colonel John Boyd Coates Jr MC USA Associate Editor Elizabeth M. McFetridge M.A. 570 pages illustrated U.S. Government Printing Office Washington D.C. 1958 Price \$6.25

This comprehensive book covers practically all phases of a difficult and controversial problem. To accumulate the vast information from a multitude of sundry reports and publications into a single volume represents a Herculean effort. Even though the title implies the work deals only with cold injuries in foot soldiers, the book also describes such injuries in seamen and aircrew personnel. The authors' threefold purpose, namely, to record the history of cold injury in World War II, to summarize what has been learned of the nature of this form of trauma, and to formulate from the materials of the past history of cold injury the principles of a sound program for its control in future military operations, has been carried out to a remarkable degree.

Early in the book it was comforting to read that the basic pathology of the several types of cold injury is the same, and that the various names apply only to the physical conditions of cold exposure. This is an advanced concept that is not generally recognized. In discussing pathogenesis, it is regrettable that a few basic research studies published since World War II and some of the older German reports were not mentioned. These investigations dispute the idea accepted by the authors that cold injury is primarily vascular and that tissue damage results from prolonged vasoconstriction. The section on clinical manifestations contains excellent photographs. The discussion of therapy, both early and late, points up the lack of standard procedures during the war and our general unpreparedness to care for these mass casualties. The chapter on epidemiology enlarges on a concept of cold injury relatively unfamiliar to many and represents a comprehensive and enlightening narration of the many factors which may or do have a bearing on the development of cold injury. This book fills a long-standing need for a single repository of material relating to a very important and difficult medical problem, primarily as it affects the military. —ROBERT B. LEWIS Col USAF (MC)

**EMERGENCY WAR SURGERY** U.S. Armed Forces Issue of NATO Handbook Prepared for Use by the Medical Services of NATO Nations United States Department of Defense Foreword by Frank B. Berry M.D. Assistant Secretary of Defense (Health and Medical) 411 pages United States Government Printing Office Washington D.C. 1958 Price \$2.25

This handsome pocket-sized handbook for the guidance of medical officers assigned to the management of individual and mass casualties of warfare is divided into four major parts: Types of Wounds and Injuries, Response of the Body to Wounding, General Consider-

at ons of Wound M n gement and Regional Wounds nd Injuries  
The quality of th material presented is excellent It is as up to date  
as the most current medic l journal nd at the same time conta ns  
the most carefully selected and worked o er technic and doctrine  
dev loped i the two world wars and in Kore

In any armed conflict all m dical offic rs in forward reas hould  
have a personal copy of this handbook A a result of the r viewer s  
personal exper enc with a sim lar Army technic l bulletin in Korea  
it is ant cip ted th t this handbook would be o e of the med cal of  
ficer s mo t valuable possess ons at the fro t If possible th s re  
viewer suggests th t the cover and text p ges be made of w ter res t  
ant mat r al nd also that an tom c drawings of surg cal approaches  
to vessels be dded to the gloss y W r surg ry taxes the ever-fad ng  
memory for a atomy as no other surg ry can

—ROALD N GRANT C M MC USN

THE YEAR BOOK OF CANCER (1957-1958 Y Book S ) comp led and  
d t d by R d lpb L Cl k J B S M D M S (Surg ry) D  
Sc (H ) d R H W Cuml y B A M A Ph D 523 p g  
Il t t d Th Y Book P bl h I Ch cago Ill 1958  
P \$8

The volum us material publish d this year h s ben creened  
by an oust nd g ditorial bo rd and th use of the uthors own  
*opinions in abstr ctng the rt cles has helped clarify th r intent*  
M t of the l t r ture being wr tt n about cancr is in the English  
langu ge nd the ed tor attribute this to the o-called cr h p gram  
on anc r that i being developed in the Un ted Stat s The articles  
aga n stress that lthoug preop r t e care surgic l technic and  
postop rative care ha e hown mpovement the v r-all cure rate  
of such malignancie as c c r of the pancre s stom ch gallbladder  
l e and lung h n t mpoved in th past dec d Two fe tures  
that ga n shoudl mpess the clin c n e tho e of arl r diagnosis  
and p e t v s gery potentlly mal gn t lesion until the v st  
expenditures o es arch find a bett r way to t eat thi disease An  
te est ng c mment ry o th progess of cancer research and tre t  
ment i Russ concludes this v ry int est ng revl w

—SHAKEEB EDE Capt MC USN

FRACTURES AND OTHER INJURIES by th M mbe f h F tur Cl  
f th M sa hus t Ge ral H p t l d f th F ul y f th Harv d  
M d cal School d d by Edw F C M D Dr w g by M n l  
M Lat b M ll Phot gr phy by D ld W th Ed t l B ard  
J ph S B r M D B dford C on M D Cl ud E w l b M D  
J m C W b t M D d Edw F C M D 863 page Il trated  
Th Y Book P bl h I Ch cag Ill 1958 P \$28

This book is a compendium f th m ter l presented each fall t  
the Massachusetts Gen al Hospital in a course entitled Treatment  
of Fractures ad Other Traumatic Conditions The various chapters  
have been w rten by th large and d st ngu shed f culty f r th s course  
39 contributo all with the former chief of the fracture service  
Dr Edw n Cave p nc pal contributo and ed tor

[illegible]

In addition to a discussion of the various fractures and their treatment, there is an interesting history of the fracture clinic of the Massachusetts General Hospital, from its foundation by Dr. Cannon in 1871 to the present, including an outline for the organization of a fracture service, a discussion of the metabolic errors of healing, studies of fractures bone grafting, comminuted fractures, etc. etc. This is an ambitious undertaking in a volume of 72 pages, and the "editors" are here and it isn't analyzed or criticized. Dr. Cannon's statement in his chapter on facial injuries that "it is not our purpose here to discuss all the methods that have been used in treating facial fractures" is very relevant to report none that have proved simple and effective. I found up this volume better than any work of this nature. It has been accomplished in a brilliant manner.

The format is good, print is pleasant and easy to read, the binding is excellent and reproductions of x-ray and draw are outstanding. This book is heartily recommended to all physical therapists who treat trauma.—WILLIAM S. STRICKER, Charleston, W. Va.

ELECTRON MICROSCOPIC FILMS OF TOPICAL LIPID LIQUIDS  
BLOOD by Fark Low Ph.D., and J. M. A. F. Farnham, B.Sc.  
Illustrated The Black and White Division of the I. Book Company Inc.  
New York, N.Y. 1967 Price \$2

This atlas adds much to the study of the morphology of blood and as there is no comparable book on this subject it will be a source of reference for a long time in this developing field. To the user of the light microscope it adds to and strengthens the interpretations already accepted and will give stimulus to further work and better correlations. The volume consists of 226 micrographs. Fourteen of these were taken with the light microscope while the remainder were taken viewed through the electron microscope. The light photomicrographs are for comparison and to guide the reader into the forest of detail revealed by the electron microscope. The index is clear and concise and provides enough information for a clear understanding of the purpose of the atlas, the techniques and materials used. The entire atlas is well planned with full photomicrographs on the right hand page and a short clear description on the left page. Each photograph is clearly marked and labeled so that the description or the label can be followed easily. It is not necessary to turn pages or to turn the atlas upside down or sideways to find the previous illustration. The photographs are excellent and the descriptions are clear. The index is simple and clear. —J. C. WELLS, JR., Col. MC USA

DISEASES OF THE THYROID AND PARATHYROID GLANDS by *Bernard J. F. Fra.* A B Sc B M D D S F word by *Arnold S. Jackson, M.D.* 295 p g Il t d l t ent l M d l Book C rpor t on N w York N Y 1958. P \$8 50

This volume on disorders involving the thyroid and parathyroid glands is written by a surgeon and is of special interest for the general surgeon concerned with thyroid surgery. The greater portion of the book is concerned with hyperthyroidism in all its manifestations and with its treatment. The use of radioactive iodine both as a diagnostic aid and as a therapeutic agent is carefully reviewed. There is a discussion of the technical aspects of thyroid surgery. The chapter reviewing thyroid cancer constitutes a rapid review of the subject. Parathyroid disease is rather briefly covered. The book is well written and illustrated and contains an excellent bibliography. This volume is recommended as a vehicle for office review of the subject of thyroid diseases. —JOHN E. GORMAN, Capt, MC, USN

ALCOHOLISM by *Arnold Z. Pfeffer, M.D.F.* word by *S. C. Fra.* M.D. F.A.C.P. 98 page Il t ted G & S I N w York N Y 1958 P \$6 50

This monograph is intended to serve physicians as a handbook for the management of alcoholic patients. It is especially aimed at the needs of the physician in industry where the occupational features of alcoholism are more easily seen. The volume presents a concise introduction to alcoholism, including definitions, etiology, and a general discussion of complications, diagnosis, prognosis, and treatment. There are five well-planned chapters and a total of 91 references. The adjunct to treatment and procedures for alcoholism including the use of the newer tranquilizers are quite adequately covered. Since the psychological attitudes and Alcoholics Anonymous. The Consolidated Edition, New York: University Bellvue Plan is discussed in detail. Program for large and small companies and additional source of assistance to those interested in doing something about the alcoholism problem and trying to solve it elsewhere are also presented. Some reasons for the late acceptance of the Consolidated Edition company procedure on alcoholism would appear to be not only the forthright acknowledgment of the problem, but also a well-defined company policy which forms the practical basis for administrative procedures to cover (1) early recognition (2) rehabilitation and (3) a consistent method for termination of employment when efforts to effect rehabilitation are unsuccessful. The program is a studied effort to uncover the alcoholic hidden man and to offer him necessary help along with the judicious application of company probation. I recommend this monograph as much to have not only for all members of the medical profession but also for all those who are interested in the problem of alcoholism and what can be and is being done about it today.

—PHILLIP B. SMITH, Lt. Col, MC, USA

NOV 1958  
SCIENCE AND PSYCHOANALYSIS Volume 1 Integrative Studies edited  
by Jules H Masserman M D 201 pages illustrated Grune & Stratton  
New York N Y 1958 Price \$5 75

This interesting book contains papers on the scientific aspects of psychoanalysis as well as the transactions related to science and psychoanalysis of the newly formed Academy of Psychoanalysis. Among the contributors are such well known names as David Mch. Rioch Roy A Grinker Abraham Kardiner Kenneth E Appel Percival Bailey and Sandor Rado. The thinking prevalent in this volume is an attempt to unify psychoanalysis with other sciences and as may be expected at this early stage the differences of opinion expressed are substantial. Some aspects of biological and anthropological psychoanalysis are discussed and the whole problem of communication defects is presented in an interesting manner. Criteria and methods have been developed in recent years that have made possible a preliminary operational investigation of symbolic behavior through the use of data from studies on verbal behavior anxiety and on certain aspects of the phenomena generally included in the concept of the unconscious. On the other hand it is noted that the superior capacity of the acculturated human being for symbolic behavior adds to the difficulty of investigating human biology by operational methods. This is a book for the advanced student. Perhaps as more work is done on the subject the material will be available in a form suitable for wider dissemination. —STEPHEN MOURAT Lt Col MC USA

CLINICAL INTERPRETATION OF LABORATORY TESTS by Raymond H Godale M D 4th edition 758 pages 105 illustrations 6 in color F A Davis Co Philadelphia Pa, 1958 Price \$8 75

This book is divided into two parts. In the first part is a brief background of physiology normal values and the significance of abnormal values of the various body fluids. One may look up sodium and find the normal values in blood a short dissertation on physiology and listings of conditions in which the value is increased or decreased. The same may be done for chlorides and so on. Part two takes by disease the various systems with the associated laboratory findings. Reference may be made to a specific disease, for instance Wilson's Disease. Under this heading a short description and listing of laboratory examinations with the findings is given. The presentation are brief as one would expect but references are available after each chapter. The index is a general one and is fairly complete. This book is recommended for the use of medical students interns and the practitioners who by necessity cover the wide field of medicine.

—JOE M BLUMBERG CL MC USA

PEDIATRIC SURGERY by Orva Swanson M D F A C S Fotedar by William E Ladd M D 750 pages 980 illustrations Appleton Century-Croft Inc New York N Y 1958 Price \$20

This new textbook is an authoritative supplement to general surgical books dealing with adult surgery. It contains an adequate description of the differences between infant child and adult as to responses to surgical procedures problems of fluid and electrolyte balance.

## CEREBRAL VASCULAR DISEASES T

H l d d h A p of h A m H t A t P c to  
 N J J uary 16-18 1957 Irv g S W ght Ch ma Cl k H M l k  
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 D 224 pag P bl h d f Th Am H t A  
 by G un & St tt In N w Y k N Y 1958, P \$4

## BRITISH MEDICAL BULLETIN V l m XI Numb 5 Sep mbe 1958

Oph h Im L t ur f 1957 d d by S St t D ke-Eld  
 G C V O C t t Ab t t f m t l t tur 562 p g  
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## BRITISH MEDICAL BULLETIN V l m XII Numb 1 Spt mbe 1958

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## POISONING A G f Cl l D g d T e tm t by W F

O t t g M D Ph D 2d d t on 6 7 p g W B Sa d C m  
 p y Ph l d lph P 1958

## TECHNIC AND PRACTICE OF PSYCHOANALYSIS by L J S l M D

244 p g J B L pp t C mpany Ph lad lph Pa. 1958 P \$8

## ESSENTIALS OF PEDIATRICS by Ph l p C J an A B M D F H uell

Wright B S M D and Fl G Bl k R N M A 6th d t on  
 14 pag ll ed J B L pp Company Ph lad lph P  
 1958 P \$6

## UROLOGY IN GENERAL PRACTICE by F ank C l m H m M D M S

F A C S d S d y R W berg M D F A C S 293 p g  
 H d J B L pp t C mpany Ph lad lph a, P 1958 P  
 \$6

## THE PHYSICAL TREATMENT OF VARICOSE ULCERS A Pt 1 M 1

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 Adj t T arne t by T War h m M C S P 125 pag  
 H t d Th W l l m & W l k C mp y B l t mor Md 1958  
 P \$4

## MONOGRAPHS ON NEOPLASTIC DISEASE AT VARIOUS SITES G 1

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 Md 1958 P \$10 50

## OUR CHILD'S WORLD by R b rt Od mu ld M D 211 p g Rand m

H l N w York N Y 1958 P \$3 50

## PASSING PHARMACY PROFITS by F t T J m 148 p g J B

L pp t C mpany Ph lad lph P 1958 P \$4 75

## SERIAL AND MYCOTIC INFECTIONS OF MAN d d by Ren J

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 d 820 p g ll at d J B L pp t C mp y Ph lad lph  
 f 1958 P \$8 50

## CLINICAL PARASITOLOGY by D d L B ld g M D 460 pag

ll ed Appleton-Cen ry-C f In N w York N Y 1958

- GUIDE TO RUSSIAN MEDICAL LITERATURE** Editors *Scott Adams*  
National Institutes of Health and *Frank B Rogers* M D National  
Library of Medicine 89 pages Public Health Service Publication  
No 602 U S Department of Health Education and Welfare Public  
Health Service Washington D C 1958 For sale by the Superintendent  
of Documents U S Government Printing Office Washington D C
- TUMORS OF THE ORAL REGIONS** edited by *Hamilton B G Robinson*  
D D S M S 143 pages illustrated W B Saunders Company  
Philadelphia Pa 1958
- THORAX** Volume 13 No 3 September 1958 edited for The Thoracic Society  
(President *P R Allison*) by *N R Barrett* and *J G Scadding* 173  
250 pages illustrated Published by British Medical Association  
Tavistock Square London W C 1 England Price \$10 00 yearly sub-  
scription (4 numbers) single numbers \$2 50
- SCHIZOPHRENIA** by *Manfred Sakl* M D with a foreword by Professor  
*Harold H J* Head Department of Neurology & Psychiatry University  
of Virginia 335 pages Philosophical Library Inc New York N Y  
1958 Price \$5
- PSYCHOLOGICAL STRESS** by *Irving L Janis* Ph D 439 pages John Wiley  
& Sons Inc New York N Y 1958 Price \$6 95
- DIAGNOSTIC BACTERIOLOGY** by *Isabelle G Schaub* A B M Kathleen  
*Flynn* M A Elvy G Sott M T (ASCP) and *W Robert Bailey*  
Ph D 5th edition 338 pages illustrated The C V Mosby Company  
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# Medical Journal



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# UNITED STATES ARMED FORCES MEDICAL JOURNAL

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## Monthly Message

In the London *Daily Telegraph and Morning Post* of Wednesday 9 July 1958 there was a half column article with prominent headlines "Boy Left for 20 Minutes After an Operation Coroner Critic". The article then described a boy of 16 who was left unattended in a side ward following a tonsillectomy. 20 minutes later he was dead. A verdict of death by misadventure was recorded on the board. Dr Gilbert Forbes, pathologist, said death was due to respiratory failure from an unknown cause. In the course of the article it was stated that the anesthetist said he took no responsibility for the patient after handing him over to the nursing staff. The coroner's comment: "I would have thought the common sense view was that the person responsible for making a person unconscious should have been responsible for him until unconsciousness had worn off."

At the time he was placed in the ward his condition was described as good with full and regular pulse and the anesthetist expected him to be watched and proper measures taken to ensure a clear airway. The nursing staff stated that there was no particular reason for the boy to have been put in the side ward. The nurse in charge took a look at him and then went to lunch. When she came back he was dead. The assistant head of the nursing office said that although ideal it was not always practicable to watch all patients recovering from an anesthetic and stated that could be left to the Sister in charge.

The above act emphasizes the importance of personal responsibility. The more a municipality, state or Federal government dilutes that sense of responsibility, the more the sense of personal care and responsibility dwindles. These faults are so easy to justify. "It wasn't my job." Every doctor must always accept decision and personal responsibility and owes it to his patient to treat him as he would like to have himself or a member of his family treated. Whether it be for simple vaccination or major surgery, he should ensure that every safeguard possible has been provided and not leave it to the enfolding arms of the organization.

*Frank B Berry*

FRANK B BERRY, M.D.  
Assistant Secretary of Defense  
(Health and Medical)

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# Foreword

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# UNITED STATES ARMED FORCES MEDICAL JOURNAL

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Number 12

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## PALPABILITY OF THE LIVER EDGE IN HEALTHY ADULTS

EDDY D. PALMER *Lieutenant Colonel MC USA*

**U**NCERTAINTY over just how far below the costal margin the right lobe of the adult liver may normally extend seems to be common. Judging from requests for gastroenterologic opinion, discovery that the liver edge descends a centimeter or two below the right costal margin is rather widely considered a sign of liver abnormality. Perhaps one reason is that most textbooks are noncommittal about the normal location of the inferior hepatic edge or ignore it completely. A few encourage distrust of the palpable liver. "Usually the presence of a palpable liver edge below the costal margin indicates either ptosis or enlargement."<sup>1</sup> "the lower border (of the liver normally) extends to the edge of the right thoracic cage."

The location of the lower edge of the liver does not, of course, necessarily bear a relationship to the size of the organ, and obviously one must determine the position of the liver's cephalad limit by percussion before hepatomegaly can be diagnosed. Nevertheless, whatever the liver's size, its upper surface is remarkably constant in its location, and diffuse hepatomegaly manifests itself almost wholly in the downward direction. Conversely, any great degree of extension of the liver's edge below the costal margin almost always indicates hepatomegaly. The main exceptions are found in cases of severe pulmonary emphysema and in true ptosis of the liver. This last phenomenon can exist only if hepatophrenic contact has been broken and the liver's suspensory ligaments are greatly elongated.

The present study was made to determine the range of positions occupied by the inferior border of the liver's right lobe,

as judged by palpation in a group of normal adults. It seems strange that in this day of isotopic medicine information is so very sparse on this fundamental point of physical anatomy.

### MATERIAL

Observations on the liver were recorded during personally conducted complete routine physical examinations of military personnel and data were compiled on 1 000 subjects who were judged to have no liver disease. Most of the examinations were either annual physicals or separation physicals with fewer re-enlistment preflight special assignment or retirement physicals. Personnel who indicated suspected illness involving the torso were excluded. Similarly, an occasional patient who was not able to relax sufficiently for a satisfactory abdominal examination had to be excluded.

It was of course essential that instances of liver disease be recognized and eliminated. A negative history and when the liver could be palpated a sharp smooth and normally firm edge were insisted on for inclusion in the study. In addition, liver function tests were carried out on subjects with the larger livers and needle liver biopsy specimens were obtained in 11 cases about which there was some question of normalcy. Some cases of chronic liver disease were recognized in the course of these routine physical examinations and were excluded.

### POSITION OF INFERIOR HEPATIC MARGIN

Special attention was paid to examination of the liver and there is no question but that many of the potentially palpable livers would have been overlooked if this had not been a special study.

The lower edge of the right lobe of the liver which is normal or is diffusely enlarged parallels only in a very rough way the line of the right costal margin. Near the body's midline the liver edge swings across to the left at a level which is quite far below the xipho-gladiolar junction. Normally then the edge and surface of the liver are exposed well below the rib cage within the subcostal angle and this is so even during forced expiration. Because in this area the liver is overlaid by the rectus muscles and associated tendons however, palpation here for judgment of liver size and consistency is notably unreliable.

It is necessary then to be very precise about the point at which the measurement is made when recording liver size on the basis of the position of its edge. The best point for the determination lies along a line just lateral to the right rectus muscle margin in the linea semilunaris. This strictly anatomic criterion for the vertical line of palpation is considerably more consistent as a guide regardless of body build than is the midclavicular or nipple line. Even in very flabby people the linea semilunaris can usually easily be located by having the supine patient raise

his head while keeping his shoulders where they are, and this is a good first maneuver for palpation of the liver

The measurement must be made at the peak of the deepest inspiration that the subject is able to take, when he is relaxed, with thighs and knees flexed. It is important that the examiner assure himself that the subject has made a maximum effort and, most important, that the inspiration has been made with the mouth open. Almost all people find that, after a full breath has been taken through the nose, merely opening the mouth permits noticeable further descent of the diaphragm.

As for the mode of palpation itself, it can only be said that descriptive comment is wholly insufficient—every doctor must find out for himself the way of using the hand which for him proves most fruitful. Probably the two commonest mistakes in technic are too heavy palpation and beginning palpation at the costal margin rather than far down on the abdomen. Some young men, it must be noted, seem to lift the chest wall off the liver at the end of inspiration, and this must be recognized so that palpation will be sufficiently heavy and deep. Confusion of a tendinous inscription with the liver edge is a possibility when the subject is muscular, as palpation is carried from the linea semilunaris over the rectus muscles. An especially important habit is to make several palpatory efforts when the liver cannot be felt. It is strange, indeed, how three or four successive efforts may fail to reveal the liver edge, while the next, made in the same location, does so easily.

#### FINDINGS

When examined by the technic described, the liver edge in 42.6 per cent of the subjects could not be palpated, in 14.4 per cent it could be felt to descend to the costal margin but not beyond, in 15.0 per cent it descended 1 cm below the costal margin, in 12.9 per cent it descended 2 cm, in 8.2 per cent, 3 cm, in 5.7 per cent 4 cm, and in 1.2 per cent, 5 cm. Separation of the second category—the situation in which the edge can be felt to descend as far as but not beyond the costal margin—may seem a bit artificial because of the rather fine point in examination interpretation it interjects; nevertheless, it is being used because, of course, detection of the liver's lower margin in such cases eliminates immediately the possibility of liver atrophy.

In tables 1 through 5 the position of the liver's lower edge is correlated with the subjects' sex, age, height, weight, and configuration of subcostal angle. The last was designated arbitrarily at the time of each examination as medium (553 cases), narrow (225 cases) and wide (222 cases), on the basis merely of general impressions of and experiences with subcostal angles. It is clear that none of these factors by itself had a controlling influence over liver size, and when the individual data were reviewed no combination of possibly controlling factors was

as judged by palpation in a group of normal adults. It seems strange that in this day of isotopic medicine information is so very sparse on this fundamental point of physical anatomy.

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TABLE 4 *Palpable size of liver correlated with weight in 1 000 subjects*

Weight (lb)	Number of subjects	Relation of liver edge to costal margin (percentage of subjects)						
		% of palpable	At margin	1 cm	2 cm	3 cm	4 cm	5 cm
90-110	84	57	14	16	6	7	0	0
111-130	131	50.4	14.5	18.4	11.7	1.5	3.5	0
131-150	283	40.3	11.0	19.1	12	7.4	6.4	3.2
151-170	208	44.9	11.6	17.4	7.2	14.6	2.9	1.4
171-190	180	38.4	16.7	10.0	16.7	10.0	8.3	0
191-210	63	79	14	5	29	5	14	5
211-230	36	50	25	0	17	3	6	0
231-250	15	0	60	27	13	0	0	0

TABLE 5 *Palpable size of liver correlated with configuration of subcostal angle in 1 000 subjects*

Subcostal angle	Number of subjects	Relation of liver edge to costal margin (percentage of subjects)						
		% of palpable	At margin	1 cm	2 cm	3 cm	4 cm	5 cm
Narrow	225	55.6	11.1	14.7	9.3	5.3	4.0	0
Medium	553	41.8	13.6	14.6	11.9	9.4	7.6	1.0
Wide	222	31.5	18.5	16.2	15.9	8.1	7	4.1

suggested. The distributions were haphazard. Apparently healthy old people do not tend to have larger or smaller livers than healthy young people; the liver is not more or less likely to extend below the costal margin in men than it is in women; et cetera.

### COMMENTS

It must be emphasized that for the clinician's purposes the configuration and consistency of the liver's edge often are considerably more helpful than its size. As previously pointed out,<sup>3</sup> discovery on routine physical examination that the liver extends a couple of centimeters or more below the costal margin and that—in particular—its edge is blunt and hard is the means by which many cases of chronic hepatitis are detected. In the present series of normals the liver edge was judged to be sharp and normally firm as a criterion for inclusion in the study. It was thought that instances of liver disease were effectively excluded both by the examiner's impression upon palpation and by the results of liver function tests and biopsy carried out in cases in which the question arose.

Findings on any routine examination are static findings indicating only conditions that exist at the moment. The exami-

nations recorded here were made at various times throughout the day. The normal adult liver which weighs about 1 500 gram contains about 800 ml of blood. The blood content therefore exerts an important influence over liver weight and size. Because presumably this blood fluctuates with the phase of digestion and physical activity it must be supposed that liver size may vary significantly from hour to hour during the day and perhaps from day to day. This matter has not yet been explored but will be

## SUMMARY

To find figures which might be useful for the clinician in his thinking about normal limits of the liver's descent below the costal margin, observations were made on the position of the liver edge during routine physical examinations of 1 000 adults. Precautions were taken to exclude subjects with liver disease.

It was found that at the point of maximum inspiration the liver edge could not be palpated in the linea semilunaris in 4° 6 per cent of the subjects descended to but not beyond the costal margin in 14·4 per cent descended 1 cm below the costal margin in 15·0 per cent 2 cm in 1° 9 per cent, 3 cm in 8° 2 per cent 4 cm in 5·7 per cent and 5 cm in 1° per cent. No correlations could be found between the position of the liver edge and the subjects sex, age height weight or subcostal configuration.

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### IMMUNIZATION REQUIREMENTS FOR TRAVELERS

Imm unization Information fo r Internat ional Travel Public Health Service Publication No 384 re ised to June 1958 has recently been published by the U S Dep rtm nt of Health Ed cation nd Welfare Copies may be obt n d from the S perintendent of Documents U S Government Printng Office Washingt n 25 D C for 30¢ e ch Th booklet co t s inf rmation on v ccin tion requirements of foreign countrie nd for entrance into th Un ted St tes recommended immunizations for the tra el t s own protectio international vaccination certificates and the loc tion of yellow fever v cc n tion centers

# MEPROBAMATE TOXICITY

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**N**UMEROUS reports in the recent literature have emphasized the value of meprobamate \* a new tranquilizer, in the management of neuropsychiatric problems, particularly those associated with anxiety and tension. The agent also has been used with very encouraging results in the treatment of both acute and chronic musculoskeletal conditions resulting from a variety of clinical disorders among which are rheumatoid arthritis and spondylitis, fibrositis, cervical root syndrome, acute and chronic torticollis, low back muscle spasm, osteoarthritis of the hip, acute active poliomyelitis of the spinal type, and tension headaches. In addition, some enthusiasm has developed for its use in the therapy of both acute and chronic alcoholism.

Review of the published data regarding the drug's toxic effects reveals the following among the more commonly observed untoward reactions: (1) dermatological problems,<sup>1-12</sup> consisting of erythematous maculopapular and vesicular eruptions in various combinations, urticaria and angioneurotic edema; (2) fever and arthralgia usually in conjunction with the skin manifestations and frequently suggesting a serum sickness type picture. Of less frequent occurrence are nonthrombocytopenic purpura<sup>13-15</sup> sometimes seen in association with the other dermal eruptions; diarrhea; temporary paralysis of extraocular muscles with diplopia; bronchospasm; acute cerebral excitation, mild hypotension, and syncopal attacks.<sup>3, 11, 2</sup>



emphasized the relative absence of toxicity and serious side effects when the agent is used at a therapeutic level. The impression often has been created that meprobamate is an altogether safe medicament. An early study<sup>2</sup> reported a case where the ingestion of 90 grams of the drug in a short time produced only marked sleepiness. In discussing three patients who swallowed 6, 10, and 18 grams of meprobamate respectively with suicidal intention, Dixon<sup>3</sup> stated that all three gave the same clinical appearance of a deep stuporous state showing hyporeflexia and mild pupillary dilatation with poor light response. All three patients responded to painful stimulation, exhibited normal respiration, blood pressure, pulse, and oxygen exchange, and recovered fully in 4 to 6 hours, requiring only physical and caffeine stimulation. Charet, Brill, and Ello<sup>4</sup> reported a suicidal attempt and mentioned four other cases about which they obtained knowledge through a personal communication with Berger. The dosage involved varied from 9.6 to 40 grams. Although the former dose produced somnolence, the 40 grams were stated to have produced no serious adverse effects. In reviewing the literature, Powell, Mann, and Haves<sup>5</sup> found 11 cases of attempted suicide with large doses.

A few recent articles, however, have uncovered the drug's more dangerous potentialities. Coma associated with hypotension has been reported.<sup>6</sup> In one of the patients the pulse and blood pressure could not be obtained and respiratory paralysis occurred.

Meprobamate is not believed to be habit forming, but Mohr and Mead<sup>7</sup> recently reported a case of apparent addiction in an alcoholic patient.

We recently attended three patients who had taken overdoses of meprobamate with suicidal intent. They are believed to be of interest not only because of the severe, prolonged coma which occurred in two with a near fatality, but also because of the striking peripheral neuropathy which developed in one of the patients.

### CASE REPORTS

**CASE 1.** A 28-year-old woman was admitted to this hospital on the morning of 8 November 1956 in a deeply comatose state. She had been under psychiatric therapy for an anxiety and character disorder manifested by passive dependent reaction and depression. On the night of 7 November she attempted suicide by taking an overdose of meprobamate prescribed in conjunction with her illness and was found unconscious in her bed the following morning and rushed to the emergency ward. After careful search of her environment and subsequent interrogation of the patient, it was determined that she had swallowed about 23.6 grams of the drug.

Physical examination on admission revealed a well-developed, well-nourished white woman who appeared deeply comatose and areflexic.

Her pulse rate was 120 per minute and thready and her blood pressure was 74/50 mm Hg. Her pupils were widely dilated and the pupillary and corneal reflexes were absent. The pharynx and nasal passages were filled with thick secretions. Rhonchi were heard throughout both lung fields. The remainder of the examination was negative.

Laboratory data revealed an initial white blood cell count of 20 700 per  $\mu$ l with 95 per cent neutrophils, 4 per cent lymphocytes and 1 per cent monocytes. The hemoglobin was 12.7 grams per 100 ml and the hematocrit was 40 ml per 100 ml. The sedimentation rate was normal. Four days after admission the white blood cell count had dropped to 9 100 per  $\mu$ l and showed a normal differential smear. The hemoglobin was 13.3 grams per 100 ml and the red blood cells numbered 4 800 000 per  $\mu$ l. The sedimentation rate had climbed to 48 mm per hour. Urinalysis on admission was negative but on the following day revealed a trace of albumin and 10 to 15 red blood cells and 10 to 15 white blood cells per high power field. Blood chemistry studies the day after admission showed normal carbon dioxide combining power, creatinine and urea nitrogen. Blood drawn on the day of admission and gastric aspirant were both negative for the presence of barbiturates. The urine was similarly negative for barbiturates and salicylates.

A dextrose saline venoclysis containing levarterenol bitartrate was promptly started. The patient's stomach was thoroughly lavaged and aspirated—approximately 12 hours after ingestion of the drug. Aspiration of the upper respiratory passages with a suction machine and insertion of a Foley catheter also was quickly accomplished. The patient was placed in an oxygen tent and given penicillin intramuscularly.

Five hours after admission to the hospital the patient was able to maintain her blood pressure without levarterenol bitartrate and its administration was discontinued. About 11 hours after admission 2 ml of picrotoxin were given intravenously, followed by an additional 2 ml 20 minutes later and then by 3 ml 15 minutes afterward. A slight eyelid flutter after the last dose was the only response. Two injections of caffeine sodium benzoate were given at four hour intervals after the picrotoxin without noticeable effect. About 12 hours after admission the patient was still deeply comatose and areflexic and showed a gallop rhythm on auscultation. There was no evidence of hyperloquemia however and the parenteral infusion was continued slowly. The gallop rhythm disappeared spontaneously one and one half hours after its initial detection.

On 9 November after approximately 24 hours of hospitalization the patient was found to be markedly dyspneic. Examination revealed coarse rales and rhonchi throughout the entire right lung, and dullness to percussion and absent breath sounds over the left lower lung field. It was thought she had partial atelectasis of the left lung. The nasopharynx was filled with thick secretions and it was obvious that frequent suctioning throughout the night had not succeeded in maintaining an adequately clear airway. A tracheotomy was consequently

decided upon. While waiting for the necessary equipment the patient suddenly stopped breathing and became cyanotic. An emergency tracheotomy was performed immediately and the tracheobronchial tree aspirated through the incision removing large amounts of unusually thick and sticky secretions. The breath sounds became audible over the left lung field and the respirations and color improved rapidly. The penicillin dosage was increased and streptomycin sulfate was added to her therapeutic regimen. A roentgen gram of the chest at that time revealed an extensive pneumonic process in the right upper lung field. An electrocardiogram showed low to inverted T waves in leads II, III, aVF and V through V with associated depression of the ST segment. Shortly afterward all her reflexes returned and approximately 32 hours after admission and 45 hours after the ingestion of the meprobamate the patient began responding to stimuli and was fully conscious four hours later. Her recovery was uneventful thereafter. The tracheotomy tube was removed four days after its insertion. The lung fields became clear and the electrocardiographic tracings reverted to normal. The patient was discharged in good physical condition and psychotherapy was continued on an outpatient basis with excellent results.

C. 2. A 19-year-old enlisted man with previously excellent record of conduct and good health was being seen at the mental hygiene clinic of this hospital because of a recent onset of bitemporal headaches and extreme nervousness and anxiety manifested by insomnia and feelings of compulsion to vigorous motor activity. A prescription for meprobamate with usual dosage schedule was written on 7 September 1956. The youth was found unconscious on the floor of his barrack in the early morning of 11 September with a suicidal note beside him. There also was evidence of considerable vomiting and two empty boxes of medicine were nearby. It was believed after tracing the prescribed medication and subsequent interrogation of the patient that he had taken 20 gram of meprobamate and an undetermined though seemingly not dangerously excessive number of acetylsalicylic acid tablets.

The patient was rushed to the hospital where initial examination revealed a well-developed slender deeply comatose youth with a regular pulse of 140, a blood pressure of 120/70 mm Hg and a respiratory rate of 32 per minute. His pupils were widely dilated and fixed and his corneal and all deep reflexes were absent.

Admission laboratory data was as follows: white blood cell count 16,000 per  $\mu$ l with 81 per cent neutrophils and 19 per cent lymphocytes; hemoglobin 15.6 grams per 100 ml and hematocrit 48 ml per 100 ml. Two urinalyses showed 1 and 2 plus albuminuria. Microscopic examination of the urine revealed 20 to 25 red blood cells per high power field on both occasions but was otherwise negative. A urine test was negative for barbiturates but positive for salicylates (145 mg per 100 ml). Blood chemistry studies revealed a blood urea nitrogen of 16.2 mg per 100 ml and carbon dioxide combining power of 17.7 mEq per liter.

The patient was adequately lavaged and aspirated placed in an oxygen tent and given 16 ml of picrotoxin intravenously without noticeable response. A spinal fluid examination was normal. Around 0700 hours on the following morning (12 September) he was still deeply comatose and areflexic and his blood pressure dropped to alarming hypotensive levels. The urinary output had been nihil and he had been running a continuous fever since shortly after admission. Levarterenol bitartrate was added to the intravenous fluid regimen with excellent blood pressure response. Rhonchi were heard at that time in both lower lung fields and a roentgenogram of the chest showed diffuse infiltrative lesions in both lung fields particularly on the right. Fearing an aspiration pneumonia he was started on penicillin intramuscularly and streptomycin sulfate in the accepted dosage. His carbon dioxide combining power was 20 mEq per liter and serum chlorides were 114 mEq per liter. Around 1030 hours on 13 September he was able to maintain his blood pressure spontaneously and levarterenol bitartrate was discontinued. Normal equal tendon reflexes were elicited at that time. Around 1300 hours of the same day the first traces of conscious behavior were detected and by 1630 hours in the afternoon he was fully conscious. The oxygen therapy was discontinued. His urinary output improved rapidly. The urinary abnormality, i.e. albuminuria and microscopic hematuria persisted until 14 September after which it disappeared. His hemogram was now within normal limits. An electrocardiogram was interpreted as normal. His fever however continued unabated. He developed a fine maculopapular and erythematous eruption on 16 September and typical urticarial lesions on 18 September both of which disappeared during the following week.

The only physical findings of significance at the time of his hospitalization outside of his continuous febrile curve were coarse rales and rhonchi throughout both lung fields particularly at the bases. His white blood cell count differential smear platelet and red blood counts were normal and his sedimentation rate was 21 mm per hour. A chest film on 18 September showed persistence of the diffuse infiltrations in both lung fields indicative of bronchopneumonic processes. In view of the dermal lesions and persistent fever it was decided to change antibiotics and Terramycin (brand of oxytetracycline) was accordingly started while discontinuing the others. Toward the end of the second week the patient developed considerable respiratory difficulty became cyanotic and delirious and his cough and purulent expectoration increased. He maintained his continuous febrile course with an average oral temperature of 103 F. Physical signs of dullness to percussion decreased breath and voice sounds and crepitant rales were noted over the right anterior lung field at the level of the 3d to 5th rib for about 4 cm lateral to the sternum. A repeat chest film revealed a new infiltrative lesion in the outlined area. A leukocytosis with neutrophilic predominance and a markedly elevated sedimentation rate were now present. It was evident we were dealing with a severe pulmonary infection obviously unresponsive to the antibiotics the patient had received. Oxygen therapy was re-

started. More intensive study of the patient's sputum showed a florid almost pure culture of *Micrococcus pyogenes* var. *aureus* coagulase positive on three occasions with good erythromycin sensitivity. This antibiotic was consequently started in large doses on 26 September after Terramycin had been discontinued. Several blood cultures were negative. The patient's temperature curve exhibited a dramatic response with his fever beginning to subside on 28 September reaching normal levels quickly and remaining flat thereafter. This coincided with a fairly prompt disappearance of his associated symptomatology and physical findings and radiographic resolution of his pulmonary process. A few cystic areas remained in the region of the right middle lobe for several months.

About 28 September the patient started complaining of pain in the ball of his right foot and a few days later of soreness in the right calf and posterior thigh muscles. At that time he had normal tendon reflexes and tenderness to palpation over that musculature without swelling, heat or discoloration. His right foot pain rapidly became more severe and hyperesthesia developed to the point where even contact with the sheet would produce excruciating discomfort which was described as a burning sensation. Examination then revealed considerable right cicatricial palsy on straight leg raising, a right foot drop and disappearance of his corresponding Achilles tendon reflex. Coughing caused severe pain in his right foot. Some sensory loss was detected over the posterior aspect of his right thigh. In view of the sequence of events, the lack of a history of back trauma, the absence of tenderness to pressure over the back region and the negative roentgenographic findings of lumbosacral area, it was believed we were dealing with a acute neuritis of the right leg rather than spinal root involvement. The patient was given two courses of massive vitamin B therapy consisting of 1000 micrograms of Rubrimin intramuscularly every day for 10 days with a week's rest period. He was completely started and maintained on physiotherapy for about two months. His discomfort gradually subsided over a period of two weeks and he showed considerable though gradual improvement in his peroneal palsy. He was evacuated to Valley Forge Army Hospital where both psychotherapy and physiotherapy were continued with further overall improvement in his condition and he was discharged to duty with minimal improvement in limitations.

**Comments.** The role played by the ingestion of salicylates in the initiation and maintenance of this patient's comatose state deserves careful scrutiny. The patient claimed he had consumed a considerable number of the prescribed acetylsalicylic acid tablets in a normal schedule prior to his suicidal attempt. He was unable to state the size of the original prescription. The dimensions of the box which had contained the tablets however indicated a maximum capacity of about 90. Furthermore the evidence of his having vomited suggested the rejection of a good portion of the drug. The urinary salicylate determination of 145 mg per 100 ml may at first glance seem like a

relatively high figure. It is known that about 70 to 80 per cent of ingested salicylates are excreted by the kidneys and that the percentage excreted bears no precise relationship to the dose administered or the urinary volume. Consequently the urinary level after a fixed dose may vary considerably depending on the urine specific gravity appearing unusually high in concentrated urine and low in diluted urine. The patient's repaired urinary output during the first 24 hours following his suicidal attempt must have contributed greatly to the urine salicylate level obtained. Unfortunately we have no data on his blood level, which is a more accurate and reliable criterion of the degree of salicylate intoxication. There is actually no known correlation between blood and urine salicylate levels where the urine salicylate concentration is expressed as milligrams per 100 ml in a random sample.

It is believed that this patient's clinical picture was not indicative of significant salicylate intoxication. Tinnitus and auditory nerve involvement are frequent manifestations of moderate or severe salicylate poisoning. These were conspicuously absent in our patient. A disturbance in acid base balance is a constant finding in salicylate poisoning. This is particularly pronounced in the more severe intoxication, a situation that would exist were a prolonged comatose state etiologically related to salicylate overdosage. The blood chemical data in the early stages of the intoxication are characterized by low carbon dioxide levels and serum pH values in the high normal or alkaline range, or respiratory alkalosis. This abnormality is thought to be a result of hyperventilation mainly hyperpnea due to a specific action of salicylate in stimulating the respiratory nervous mechanism. In more severe poisoning this initial respiratory alkalosis is followed by a true metabolic acidosis with primary carbon dioxide and alkali deficit, marked reduction of buffer base and a shift of the serum pH from the alkaline to the acid side of normal. This later phase acidosis incidentally is most probably caused by organic acid metabolites<sup>23</sup> arising from changes in the intermediary cellular metabolism resulting from the action of salicylates rather than the salicylate radical itself. Ketosis with acetonuria is commonly encountered at this stage. It is obvious that our patient did not exhibit a comparable clinical picture. His initial hyperventilation was more in the nature of tachypnea rather than hyperpnea and its duration was short. It may be claimed that meprobamate might have interfered or modified this characteristic respiratory manifestation. No serum pH studies were made. His blood carbon dioxide was somewhat low on the day of admission (17.7 mEq per liter). However this returned to normal levels during the following 24 hours despite the fact that he did not receive any alkaline fluids parenterally and remained so thereafter. This becomes

rather convincingly against the development of any significant degree of metabolic acidosis

C 3 A 23 year-old enlisted man with a severe emotional instability reaction received a prescription for 25 meprobamate tablets (total of 10 grams) on 14 November 1956 as part of his therapeutic regimen. On 15 November at about 0500 hours he swallowed all 25 tablets ate breakfast and reported for an appointment at the clinic at 0800 hours. He appeared confused and in an obvious state of drug intoxication. He admitted taking the overdosage of the drug and was rushed to the hospital's emergency room. His stomach was immediately aspirated and lavaged—approximately four hours after swallowing the meprobamate.

Physical examination on the ward revealed the patient to be a slender well-developed Caucasian who was markedly lethargic but could be aroused. His pulse rate was 96 per minute and regular and his blood pressure was 100/80 mm Hg. Except for the lethargy and generalized muscular weakness the physical examination was otherwise negative.

The laboratory data were as follows: white blood cell count differential smear hemoglobin hematocrit and urinalysis were all normal. Sedimentation rate was 12 mm per hour. The urine and blood ammonia on admission were negative for the presence of barbiturates. A roentgenogram of the chest was interpreted as normal.

The patient was placed under close observation and given 5 mg of Dexedrine Sulfate (brand of dextroamphetamine sulfate) orally every four hours. He improved rapidly and within approximately five hours after entering the hospital and 11 hours after taking the overdosage of the drug he was alert and cooperative. After 24 hours the Dexedrine dose was reduced and after 48 hours was discontinued. The patient was discharged from the hospital in good physical condition five days after admission.

### COMA AND HYPOTENSION

The precise metabolic mechanisms involved in the production of coma and hypotension by meprobamate have not been elucidated. In animal experiments massive doses of meprobamate produce a reversible flaccid paralysis of most voluntary muscles and thereby resembles curare in its action except that the respiratory muscles are invariably spared. This is the picture usually encountered in comatose patients who have taken suicidal overdoses. Hiestand postulated that the loss of muscle tonus somehow interferes with the ability of the vascular system to maintain normal tone with consequent drop in pressure. It would be interesting in this connection to correlate the degree of muscle relaxation and deep tendon reflex depression with the presence or absence and severity of hypotension. Another mechanism however would have to be sought to explain the hypotensive phenomenon described after ingestion of one tablet.

of meprobamate with the patient remaining fully conscious and ambulatory. A direct action on the vasomotor center of the medulla is, of course, another possible explanation.<sup>1</sup>

An individual susceptibility to meprobamate is suggested by the wide variations in the dose producing serious degrees of central nervous system depression among different patients. Whereas 40 grams have been reported to have produced no serious side effects,<sup>2</sup> Allen and Black's<sup>23</sup> patient became pulseless and developed respiratory paralysis after ingestion of 12 to 16 grams of the drug, despite her early gastric lavage and probable removal of a certain amount of the agent. Also in marked contrast to the latter case our last patient merely manifested a deep slumber and was easily aroused at all times although he ingested 10 grams of meprobamate and was lavaged quite late. Dixon's<sup>23</sup> patients revealed identical clinical pictures, yet one took 6 grams while another swallowed 15 grams of the drug. Hiestand's<sup>4</sup> patient apparently never was in serious distress and showed a return of pupillary reflexes in 4 to 6 hours and good muscular response 18 hours after taking 36 to 38 grams of meprobamate. Yet of our own first two patients, one was a near fatality and the other suffered a severe 48 hour coma with prolonged hypotension after taking 23.8 and 20 grams respectively. Statements regarding the amount of drug swallowed may be subject to question particularly in view of the personality of the patients involved.

### PERIPHERAL NEUROPATHY

The peripheral neuropathy which developed in our second patient is a subject for interesting speculation. Careful review of the literature failed to reveal a single instance of peripheral nerve involvement following the use of oxytetracycline, erythromycin, or picrotoxin agents used in the patient's therapeutic management. Similarly, there is no published report of a staphylococcal infection or salicylate intoxication producing such a morbidity. Streptomycin sulfate also received by the patient is well known for its neurotoxicity. It frequently involves the eighth less commonly the third and second cranial nerves and in its incipient years occasionally produced a fatal encephalopathy when extremely large doses were being given. However as with the preceding agents there is no official reference implicating the antibiotic in the causation of such a neuropathy. In 1946 Kolb and Gray<sup>3</sup> reported seven cases of peripheral neuritis following repeated intramuscular injections of penicillin for various infections. The onset of the neuritis was observed between 10 and 21 days after the institution of penicillin therapy and in some cases, while receiving the antibiotic. The protocol of four of the seven cases mentions the injection of penicillin in the area of a nerve trunk later involved by the neuritic process. In the others there is no description



of the injection site. In 1949 Broadbent, Odum, and Woodhall<sup>1</sup> described four cases of peripheral neuritis following intramuscular penicillin administration convincingly shown to be due to nerve injury from the local drug infiltration. Several of the accidents may well have been related to impurities present in the penicillin preparations available at that time. Considering the number of years that penicillin has been in the world market and its widespread popularity, the reporting of so few cases suggests that this complication following its use must indeed be a rarity. Nevertheless, it is a possibility which should be entertained were a peripheral neuropathy to develop during penicillin therapy. It is difficult, however, to escape the conclusion that meprobamate could be implicated in its causation. The drug certainly can produce profound though as far as it is known reversible alteration in muscle tonicity and behavior through its action on intraneuronal nerve fibers. The observation is being offered for its factual value and as a reference for future elucidation.

#### THERAPEUTIC CONSIDERATIONS

In animal experiments Metrazol (brand of pentylenetetrazol) was found to be the most effective antidote to meprobamate producing a definite shortening of the comatose state. Picrotoxin proved quite ineffective. This adds credence to Heberden and Cooper's<sup>2</sup> description of their patient's dramatic response to intravenous metrazol becoming fully awake within the ensuing 60 seconds after having been in coma for many hours following ingestion of slightly over 8 grams of meprobamate. It also explains our two unsuccessful experiences with picrotoxin.

The associated hypotension has shown consistent prompt response to intravenous levarterenol bitartrate though in a few instances its administration had to be continued for many hours. Allen and Black<sup>3</sup> kept their pulseless patient with respiratory paralysis alive by using besides levarterenol cerebral electrostimulation with a Med Craft Electronic Transient Therapy Unit. This was applied over a period of three hours before the patient was able to maintain her own respiratory activity. No Metrazol was used however.

It is obvious that careful evaluation and prompt reversal of all serious threats to life as they develop should be an integral part of the patient's management and need no further comment.

There are now available a qualitative urine test for meprobamate and a colorimetric procedure for the presence of the drug in body fluid where a question of diagnosis exists in instances of coma of unknown cause.

#### SUMMARY AND CONCLUSIONS

Meprobamate has gained rapid acceptance among members of the medical profession as an effective agent in the manage-

ment of musculosprastic disorders and neuropsychiatric problems, particularly those associated with anxiety and tension. Its administration has in certain instances, however, led to some serious, even fatal reactions and uncovered its dangerous potentiality when used without judicious discernment. This facet of its toxicity was analyzed and discussed after reviewing reported instances of severe reactions with particular reference to coma and hypotension. Consideration was given to a few valuable therapeutic observations. Experiences with three patients who took overdoses of meprobamate with suicidal intention were presented and added to the discussion. The importance of exercising good judgment in prescribing the drug, especially to depressed potentially suicidal or seriously disturbed individuals, was strongly emphasized.

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### TUBERCULIN TESTING OF MILITARY PERSONNEL

Tuberculin testing now well established by the Navy is ideally suited to the needs of the armed forces as a tool for detection of tuberculous infection. This is particularly important because 90-95 per cent of recruit enter service with negative skin tests. Their duties carry them occasionally to parts of the world where opportunity for infection is great. Such infections should be service connected even if only identified by a conversion of the tuberculin test. Possibly they should be treated at this stage—perhaps the armed forces could determine for us by means of a well designed study if they need to be treated.—H. Corwin Hinshaw. Speculations on the Future Treatment and Control of Tuberculosis *D. as fth Ch st* September 1958

# MEDICAL RADIATION AND COMMON SENSE

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**S**HORTLY after Röntgen announced the discovery of x rays in November 1895 it became obvious that this strange new energy possessed some hazardous properties. By 1898 the British Roentgen Society was already collecting information on the injurious effects of roentgen rays.<sup>1</sup> Knowledge of the extent of these hazards and the degree of protection required was slowly accumulated in the years 1900-1935. By 1935 the collection of such data had been tremendously accelerated by the international acceptance in 1928 of a unit of measurement of ionizing radiation, the roentgen, and by improved instrumentation permitting accurate measurement of these units.<sup>2</sup>

Fortunately awareness that the rays were potentially harmful did not prevent the pioneers in medical radiology from developing this field as a diagnostic and therapeutic discipline. The rapid advances and developments in radiology in less than three score years have been awe inspiring, and the changes wrought upon the entire field of medicine by utilization of ionizing radiation are of immeasurable importance. For instance, Coller<sup>3</sup> has pointed out that prior to the discovery of roentgen rays surgical operations were limited to conditions that Hippocrates could have diagnosed easily.

Nearly sixty years later, a rather sudden popularization of the uses and hazards of radiation through the medium of the lay press has become a problem of great importance and concern to medical and dental practitioners. We now find ourselves treating a patient population that is confused, apprehensive, misinformed and reluctant with regard to the medical uses of x ray and radiant material. The public has been exposed to a plethora of articles by the press—some well intentioned but lacking clarity, others frankly terrifying in their approach and conclusions.

Consequently a new medical problem has arisen, the patient so resistant to the use of diagnostic and therapeutic radiation that he wishes to forego it and revert to more primitive modalities. We have seen a strong man, a former military pilot, turn

pale and tremble when told he would have several hundred roentgens delivered to a pituitary tumor. He had read that a dose of 600 r from atomic weapons produced immediate death. As a world renowned radiation physicist has put it, we have now reached the point where the hazards of dealing with the hazards are greater than the hazards.

A calm reappraisal of the hazards, advantages, protection and uses of diagnostic ionizing radiation in medicine seems in order. However, consideration of the problem of radiation effects upon the population can not and should not be limited to radiant sources utilized in medical and dental practice.

### SOURCES OF RADIATION

The population of the earth is and has been constantly bombarded with ionizing radiation. The sources of this radiation include cosmic rays, naturally occurring radioactive elements, man-made radioisotopes, medical and dental x-ray generators, nuclear fall out from atomic weapons, and industrial generators and reactors.

The major portion of background radiation (from cosmic rays, radioactive rocks and soil, and internal radiation from radioactive components of the body) cannot be effectively controlled but is variable under different circumstances. For instance, the 30-year accumulated gonadal dose of a person living at sea level in a frame house is 3 r or more. If this person moved to a similar house in Denver, the cosmic ray activity at this altitude would increase his 30-year gonadal dose by 17 per cent. Moving to a brick-concrete or stone house in Denver would increase his dose another 33 per cent. Living on the sandy beaches of Travancore, India, might produce a 30-year accumulation as high as 50 r. So far, an increased incidence of radiation injuries related to brick houses in Denver or mud huts in Travancore has not been described.

The gonadal dose to the people of Great Britain from diagnostic x-rays is reported to be only 92 per cent of that received from natural sources.

### DELETERIOUS EFFECTS OF RADIATION

The harmful effects of ionizing radiation upon the body as listed by The International Commission on Radiological Protection are:

1. Supercritical injuries
2. General effects on the body, particularly the blood and blood-forming organs, e.g., production of anemia and leukemias
3. Induction of malignant tumors
4. Other deleterious effects including cataracts, obesity, impaired fertility, and reduction of life span
5. Genetic effects

Some knowledge of these effects will facilitate clarification of patients' misconceptions regarding somatic injuries.

**Superficial Injuries** Acute superficial injury of the skin was first noted within one month of Röntgen's discovery.<sup>7</sup> Subsequently chronic effects became apparent after a latent period of varying length. Because of lack of data on the dose received by most individuals injured in the past, it is difficult to form a concept of permissible dose which precludes injury.<sup>8</sup> Doses in the order of 4 r per week have produced skin changes.<sup>9</sup> The safe tolerance dose has been given as 0.5 r a week to the surface of the body. This dose corresponds to 0.3 r a week measured in free air. It should be pointed out that the effects of overexposure of skin are, to a large extent, independent of the size of the area exposed. This is in contrast to other tissues, such as the hematopoietic system, where destruction or injury to one area may be compensated for by proliferation in another area.

Acute superficial changes, erythema and epilation require large doses in the order of 250-1000 r depending on the wave length. Chronic changes which include atrophy, telangiectasia, radiodermatitis, chronic ulceration and carcinoma require large doses over an extended period of time. With present day knowledge and equipment these injuries should not constitute a problem in diagnostic radiology.

**Effects on the Blood and Hematopoietic Tissue** Since 1903 it has been known that radiation affects the blood and blood-forming organs. There is wide variation both qualitatively and quantitatively, as to the effect on particular blood elements according to the amount of radiation, the quality and source of the radiation, the conditions under which irradiated, and the observer reporting.

Aplastic anemia has occurred in some radiologists who apparently received large doses.<sup>1</sup> It may be produced in guinea pigs with exposures of 2.2 r per day.<sup>1</sup>

Leukemogenic effects of radiation have been widely publicized. Evidence that there is a correlation between exposure to ionizing radiation and development of leukemia is overwhelming. March<sup>11</sup> observed that leukemia is nine times as frequent in radiologists as in other physicians. Henshaw and Hawkins<sup>12</sup> have reported that the incidence of leukemia in physicians is almost twice that in the population as a whole and that this may be because of the use of and exposure to x-rays and radium. Leukemia may be induced experimentally in irradiated animals.<sup>1</sup> Leukemogenic effects have been described in survivors of the Nagasaki and Hiroshima explosions and in British children irradiated as fetuses.<sup>13-15</sup> Quantitative data as to what constitutes a leukemogenic dose is lacking and no patient can honestly be told that such and such dose will increase his risk of leu

kemia Experimentally a given dose of partial body irradiation will not increase the normal incidence of leukemia in mice but when given to the entire body the incidence is increased Diagnostic radiology is practically based on partial body exposure

The literature is replete with experimental and clinical cases of radiation induced malignancy Besides leukemia there are reports of skin cancers in previously treated areas thyroid carcinoma following irradiation of the thymus during infancy and of various tumors experimentally produced in animals These occur at dosage levels which should not be encountered in diagnostic procedures or current methods of radiation therapy

**Other Deleterious Effects** Most widely known and oft quoted of these other deleterious effects are reduction of life span and impaired fertility

Information on life shortening by irradiation is derived mainly from animal experiments utilizing high dose rates or large doses In man reports have indicated that the life span of radiologists is shorter than that of other physicians or other medical specialists This has been attributed to chronic radiation exposure Recent reappraisal of these figures however does not support this hypothesis and suggests that the difference is related to differences in age composition of the groups There is no direct method of relating life span to past radiation exposure Many radiologists dying in earlier groups were older men who may have received 75 times the dose encountered by present day radiologists with modern equipment

Impaired fertility or sterility can be produced by large acute doses of radiation Irradiation of 625 r delivered in a few days to the ovaries may produce permanent amenorrhea and slightly higher doses to the testes aspermia However a complete gastrointestinal series yearly for 30 years would not produce sterility dosage levels Impaired fertility or reduction in the number of offspring as a result of radiation exposure is almost impossible to evaluate in our complex society

**Genetic Effect** The effect of ionizing radiation on the normally unchanging gene has been the prime object of much recently gained public attention Naturally occurring gene change or mutation is extremely rare but in all species thus far studied it has been found undesirable It is accepted that radiant energy along with chemicals fever and other factors increases the mutation rate Moreover there is no known lower limit of gonadal exposure at which change does not occur Thus in order to gain a reference point an estimated dose that will double the mutation rate is used called the doubling dose The Genetics Committee of the National Academy of Sciences has taken the range of 40 to 80 r to the human gonads as the doubling dose Later calculations by Glass suggest a gonadal

dose as low as 10 r may double the mutation rate. Carrying these assumptions further, a doubling dose delivered to the gonads of the country's entire reproductive age population would likely increase the present rate of genetic defects among newborns from 2 to 4 per cent.

When discussing genetic effects, it must be kept in mind that it is not possible to avoid radiation from cosmic sources and the earth. Furthermore, a given individual's dose is not the important factor but, genetically, it is the *average* to the *entire* population between conception and the end of child bearing that is critical. Diagnostic radiation to older people is of no consequence.<sup>26</sup>

**Somatic vs Genetic Effects** The difference between somatic and possible genetic damage has not been made clear by recent publicity. This lack of clarity and completeness has undoubtedly enhanced the fears, mainly unfounded, that are prevalent in the public and not a few physicians. When discussing this subject with patients, one soon observes that the most alarming misconception is an erroneous association of small genetic dosages with personal somatic harm. This strong but misguided motivation for self preservation occasionally is manifested by a patient refusing to submit to a routine chest film. Yet this same person has no hesitancy about wearing a luminous dial watch which may contribute an even greater dosage.

One must constantly bear in mind that the low dosages of radiation which the geneticists suspect may be harmful refer to gonadal dosage to the *entire* population. Many diagnostic procedures are adequately performed without measurable radiation reaching the gonads. Further, this amount of radiation has not been shown, experimentally or otherwise, to induce somatic damage to the individual.

Reassurance of an individual who is apprehensive regarding radiographic procedures is most effective when it is made clear that he or she as an individual is in no danger of harm. Most incompletely informed patients we encounter are anxious about their own health rather than that of future generations. Quimby has accurately described the present state of mind created by incomplete or inaccurate lay articles, "They (the public) do not know what they are afraid of—they are just afraid."<sup>27</sup>

The physician armed with a clear understanding of the difference between somatic and genetic hazards and with a few comparative figures can ease many patients' fears. Hodges states that evaluation of available data indicates that, with the possible exception of situations in which the gonads must be in the direct beam, diagnostic radiology conducted by qualified radiologists with proper equipment contributes an insignificant part of the total gonadal irradiation over a 30 year period when compared to existing background radiation. As far as the danger of somatic harm is concerned, the best current estimate<sup>27</sup>



regarding total whole body dosage from *all* sources received annually by the average U S citizen is 0.304 roentgen absorbed. Many times the dosage dealt with in diagnostic radiology when delivered over a period of many years has not been shown to cause detectable individual damage.

### THE MAXIMUM PERMISSIBLE DOSE

The maximum permissible dose applies to those individuals who are occupationally exposed to ionizing radiation. Details of the derivation and exact definition of this phrase are to be found in radiation protection handbooks of the National Bureau of Standards. All present values and concepts in use today regarding maximum permissible dose result from recommendations of the National Committee on Radiation Protection and the International Commission on Radiological Protection. There are many facets to this subject and for the physician a working concept is most valuable. At present the rule is that protective barriers and measures should be such as to limit radiation to workers to a maximum of 0.3 roentgens in air whole body dose per week or 210 roentgens accumulated dose by age 60.

The concept of maximum permissible dose should be applied with the understanding that the expressed limits are merely an educated guess as to the dose of ionizing radiation that in light of present knowledge is not expected to cause detectable bodily injury to a person at any time during his lifetime. The maximal permissible dose does not represent a tolerance limit. In a practice which is properly regulated and monitored it is found that radiologic personnel usually receive much less than 0.3 r per week. In our own department servicing a 900 bed hospital the average exposure to radiology personnel is less than 10 per cent of the maximum permissible dose.

Committees responsible for radiation protection handbooks stipulate that radiation exposure resulting from necessary medical and dental procedures shall be assumed to have no effect on the radiation exposure or tolerance status of the person concerned. This stand is based on the conviction that it is unwise to assume quantitative information when none exists.

Natural radiation sources contribute in the neighborhood of 0.015 r per week or one twentieth of the maximum permissible level of 0.3 r. Chamberlain described most radiations workers as receiving about 0.03 r per week, an amount which he concludes does not seem to be an excessive increase over the natural background. A properly performed routine chest film gives an absorbed partial body exposure of approximately 0.05 r and less than 0.001 r to the gonads. It is apparent that the maximum permissible dose of 0.3 r and a working actual exposure in the order of 0.03 r leaves considerable leeway for performing necessary radiographic procedures on those people who are occupationally exposed to radiation. Before being subjected to diagnostic or survey radiographic procedures the

increasing number of occupationally exposed individuals in industry, military, and medical fields will place an increasing demand upon the physician to explain the concept of maximum permissible dose in similar terms.

### RADIATION PROTECTION

The significance of radiation protection is drilled into the radiology resident during his entire specialty training period. For many years the American Board of Radiology has required applicants to be well informed in all aspects of protection. As only 4,000 of the approximately 126,000 professional users of x-ray equipment have comprehensive special training in radiology,<sup>1</sup> a brief discussion of protection is presented here.

Medical x-ray protection is directed toward elimination of all unnecessary radiation to the physician, technician, and auxiliary personnel as well as to the patient. The population may be divided into four groups, each with different problems within the sphere of avoiding all unnecessary radiation.

*Group I* Those individuals whose occupations entail exposure to radiation. As mentioned earlier, this group is increasing in number. Available evidence indicates that present dosage limits are adequate to avoid significant somatic effects.

*Group II* Those with illness (including the pregnant mother and fetus) at any age from conception to the end of the reproductive period. It is in this group that potential genetic hazards are greatest and that extra protective measures are most worthwhile.

*Group III* Those with illness beyond the reproductive period. This includes most people over 30 years of age and practically all people of 40 years or more. Genetic hazard is no longer a problem. With rare exception, as stated earlier, there is no risk of somatic damage to these individuals in diagnostic radiology. Fortunately, most patients requiring extensive diagnostic studies fall into this category.

*Group IV* The well individual. Medically, these people should receive the same consideration as the reproductive age group regardless of age. This is in keeping with the principle of avoiding all unnecessary radiation. This does not imply that early detection procedures are to be avoided. For example, a properly performed chest film (fig. 1) delivers no measurable radiation to the gonads.

Obviously, it is desirable that radiation exposure to individuals in each of these four groups be held to the minimum dose *consistent with their medical requirements*. It is important to realize that the amount of radiation consistent with medical requirements is different for each group. Furthermore, any given individual may, during his life span, fall into several or all of these groups.

I recommend that a permanent record or "radiation passport" be maintained for everyone, with every exposure noted,

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Each one of these areas is the responsibility of the physician or physicians involved for implementation. Methods by which the physician can reduce radiation exposure to the population will be considered singly and in some detail.

**Improved Techniques** The physician who studies and applies the latest techniques is doubly rewarded with improved diagnostic results as well as greatly reduced patient and staff radiation dosage.

Higher voltages with rare exception do not significantly alter the diagnostic quality of radiographs. This increases penetration of the beam while decreasing the total quanta of rays that must strike the patient to produce a satisfactory film or fluoroscopic image. Resulting films may demonstrate less contrast or eye appeal, but reduction in exposure is considerable.

Dark adaptation is emphasized in every discussion of fluoroscopy. Importance of this expedient warrants its mention again. At least 20 minutes in darkness are required to achieve complete adaptation. When red goggles are worn for this period of time in light surroundings an additional 2 to 3 minutes in a dark room are necessary to bring adaptation to maximum. If properly dark adapted the fluoroscopic procedure is performed with a smaller amount of radiation while achieving the desired results in less exposure time.

Where possible one must utilize the decrease in exposure that results from application of the inverse square law. The intensity of radiation decreases in relation to the square of the distance. In radiography this means using a minimum of 36 inches target-film distance. In fluoroscopy this means one must require tables of a design that permit a minimum of 14 inches from the tube target to table top. 18 inches is even more desirable and should be demanded of future equipment.

Irradiating the smallest area consistent with desired results not only decreases patient exposure but greatly enhances the fluoroscopic image and quality of radiographs by decreasing scatter or stray radiation. This is achieved by cones, shutter cut diaphragms. Diaphragms must be constructed to limit the fluoroscopic beam so as to leave one half inch of inactivated fluoroscopic screen of all margins with the screen at maximum distance above the table top and with the shutters fully open.

Addition of filtration in the primary beam has little effect on resulting fluoroscopic images or roentgenograms but greatly reduces patient exposure. Filtration removes a large portion of long wave length or soft radiation that is absorbed by the patient and does not reach the film or fluoroscopic screen to serve any useful purpose. The resulting beam is made of penetrating short wave length or "hard" rays. An aluminum filter to inherent tube filtration reduces by 80-85 per cent in ranges up to a 130 peak.

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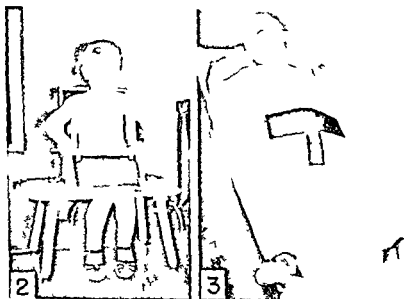


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Fig 4. L ad bb h ld d s d to prot t b th the p t t d  
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of radiation exposure. A minimum of one or two films will often produce the desired information and if not, additional films can be obtained as may be specifically indicated. Careful evaluation of the information derived from the examination is a fertile field in which to decrease patient exposure. Radiography should be performed in lieu of fluoroscopy, except for the study of cardiopulmonary physiology, or gastrointestinal examinations and a few other selected procedures. Based on figure 3 already cited, one minute of chest fluoroscopy gives a radiation exposure equal to 80 routine posteroanterior chest films when both procedures are conducted properly. A similar comparison may be made in the use of Bucky films in lieu of placereams for evaluating a pulmonary cavity.

**Patient Selection** Actually, one does not truly select the patient. However, an awareness on the part of the physician of disease incidence, age incidence and the four population groups described earlier will guide him to a degree of selectivity. This expedient for reducing exposure can be made clear by a few examples. The rapidly healing fracture of a well set bone in a child requires infrequent radiographs, whereas the old person with slower healing can tolerate frequent x-ray examinations. The young adult with a "stable" duodenal ulcer rarely needs more than an annual gastrointestinal series, but a gastric lesion needs frequent checks. On the other hand, the old adult with a duodenal ulcer should be examined frequently to can tell if his latest symptoms are not due to a new gastric lesion?

Multiple films of the abdomen should be avoided in any possible instance during pregnancy. This includes roentgen pelvimetry. Necessary pelvimetry should be performed as early in the pregnancy as possible. Examination of the abdomen and pelvis during pregnancy should be avoided except under most severe hazards to the mother's health. Other radiographic procedures, however, can be performed with shielding as near with minimum or no risk to the fetus. Multiple examination of the same area, film studies in the occupationally exposed individual, and all x-ray procedures in children should be carefully considered and frugally ordered.

## DISCUSSION

The foregoing comments are designed to bring out the salient points in a common sense approach to the probable hazards arising from the medical use of ionizing radiation. It is freely admitted that radiation is harmful as well as beneficial. Injuries to the irradiated organism may be derived from acute or chronic exposure. The same is true of many sunlight, foods, automobiles, and exercise. (2) The effects of radiation are well documented and rather well understood qualitatively. Our present knowledge does

tensive routine surveys and frequent re examinations often result from lack of initiative or experience on the part of the requesting physician. This practice is a considerable source

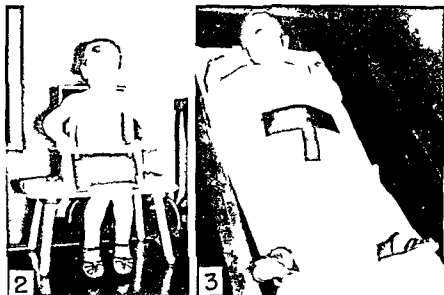


Fig 2. Lateral view of patient in chair with device attached to back. Fig 3. Lateral view of patient lying down with device attached to back. The device is a portable X-ray unit used for the purpose of obtaining lateral views of the spine for comparison with the lateral views obtained from the portable X-ray unit.



Fig 4. Lateral view of patient in chair with device attached to back. (A) Patient lying down with device attached to back. (B) Patient lying down with device attached to back. The device is a portable X-ray unit used for the purpose of obtaining lateral views of the spine for comparison with the lateral views obtained from the portable X-ray unit.

Educational material is readily available for physicians and laymen. Many excellent articles have appeared in recent medical literature. The American College of Radiology has an extensive educational and public relations program on radiation uses and hazards that is available for presentation to both professional and lay groups.

The case for education was ably stated by Dr. Richard H. Chamberlain who said:

Education of all is a continuing obligation so that our present knowledge may be extended to its fullest use. To do our work with all of the skill and care that is attainable is the most effective of all measures in radiation protection. This is not to be achieved by legislation or rigid rules by exhortation or even fear but proceeds from the individual mind which employs wisdom, experience and common sense.<sup>1</sup>

### SUMMARY

Ionizing radiation as utilized in medical radiology possesses potentially harmful as well as helpful qualities. The maximum permissible dose of 0.3 r per week or 210 r before age 60 is at best an educated guess and does not include exposure from medical and dental x-rays. The dosage from these sources is considered relatively insignificant to the entire population group when compared to background radiation that cannot be modified. Still, dosage from medical radiation should be reduced to the minimum possible levels consistent with good medical practice. Equipment and procedural methods for achieving this reduction are discussed.

Education of physicians and patients is required to overcome unreasonable fears of medical radiation which, as a result of recent publicity in the lay press, threaten to compromise use of this invaluable medical tool. The hazards of radiation exposure are known, and the means of protection are available.

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### MEDICAL PREPAREDNESS IN PEACETIME

Why is it desirable to improve our medical preparedness? Have we not always handled our medical emergencies in both peace and war reasonably well? The answers to these questions are important. If we are already doing all right then let us forget the whole thing. On the war combat side the answer is obvious: things have changed and are changing rapidly. Newer weapons of war can inflict casualties on a scale previously impossible. On the natural disaster side the answer is not so obvious but it is clear. We have not always done a good job in handling medical emergencies. Advances in medical knowledge in the last quarter century have frequently not been put to use. It is important that the medical profession realize this and further realize that a peacetime medical emergency can occur any place. We have not learned how to prevent bus, train, or airplane crashes; hurricanes, tornadoes, floods, or fires. If the local medical community will prepare itself to cope adequately with these it will have gone a long way toward preparing itself for a wartime disaster.—Silas B. Hays, *Medical Preparedness Journal of the American Medical Association* September 20, 1958.

# EFFICACY OF IMMUNIZATION AGAINST ASIAN INFLUENZA IN THE UNITED STATES NAVY

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THE far flung ships of the United States Navy have been a sensitive indicator of the spread of Asian influenza throughout the world. Ships of the Pacific Fleet began reporting epidemics in April 1957 and a high percentage had been involved by August 1957. The A/Japan/305/57 strain of influenza virus was isolated at the 406th Army Medical General Laboratory from the throat washings of a sailor of an aircraft carrier on which an outbreak of influenza occurred following the visit of the ship to Hong Kong in mid April. Sporadic outbreaks began to occur in the Atlantic Fleet as early as June 1957 but it was not until a large number of ships entered European ports during North Atlantic Treaty Organization (NATO) exercises in September and October that many simultaneous outbreaks were reported. The span of experience thus extends before and after the introduction of specific vaccines containing Asian strains of influenza virus in late August and September of 1957.

These ships have provided the Navy with an opportunity to assess the value of the vaccines made available to them. Ships of the same type are reasonably comparable in number and composition of personnel, intimacy of contact, and daily work loads. Operational assignments provide the major variable because shore contacts are responsible for the introduction of disease aboard ship. Opportunities for shore leave or the rigorousness of operations can greatly influence the willingness of personnel to report illness and the medical responsibilities for ships in port, particularly smaller ships, are often assumed by larger ships or shore dispensaries. While these factors together with other variables prevent the consideration of any one ship as a comparable control for another, the aggregate experience of a number of ships appears to have provided a negative answer to the major question of concern to the Navy: Would the available vaccines offer significant protection against explosive outbreaks of Asian influenza in operational units of the Navy?

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Comparison of the experience on ships following vaccination with the results obtained in controlled studies among recruits at the Great Lakes U S Naval Training Center<sup>1</sup> leads to the inescapable conclusion that the failure of protection on ships resulted only from the poor antigenic potency in humans of certain lots of vaccine obtained commercially

### BACKGROUND

Polyvalent aqueous influenza vaccines have been administered to all naval personnel each fall since 1954. The virus strain compositions of these vaccines have been in accordance with recommendations of the Commission on Influenza of the Armed Forces Epidemiological Board.<sup>2</sup> U S Naval Medical Research Unit No 4 has undertaken controlled studies among volunteers from the recruit population at the U S Naval Training Center, Great Lakes, Ill., in an effort to evaluate the effectiveness of these vaccines each winter. Because of the generally low incidence of influenza between 1954 and 1957 efforts at evaluation had not been particularly rewarding, either in these controlled studies or by comparison of military with civilian experience.

In May and June of 1957 extensive outbreaks of Asian influenza occurred on ships operating in the western Pacific. A high proportion of men on these ships had been vaccinated with a polyvalent vaccine six to seven months previously and many had been vaccinated annually for several years. Lacking other control measures, revaccination with the available polyvalent vaccine was advised. This vaccine, which had been used in the annual program during the fall of 1956, contained 250 CCA (chick cell agglutinating) units each of Swine, FM1 strains of influenza A viruses, and the Great Lakes 1954 strain of influenza B virus per ml. It is hereafter referred to as "1956 polyvalent."

When monovalent Asian influenza vaccines containing 200 CCA units of the A/Japan/305/57 strain per ml became available through commercial channels in late August, a special purchase of 125,000 ml was made. About 90,000 ml were immediately distributed to Navy units scheduled to participate in NATO exercises in the northeastern Atlantic and Mediterranean during September and October. Most of the balance was distributed to other fleet and shore units in Great Britain, Continental Europe, and the Mediterranean areas where influenza was spreading in civil populations, and military populations were under immediate threat. A small quantity was sent to the U S Naval Medical Research Unit No 4 at Great Lakes, Ill., for controlled studies on antigenicity and effectiveness. Thus, monovalent influenza vaccine was available in quantity only to ships and other operational units of the Atlantic Fleet. The dosage directed for personnel of such units was 1 ml subcutaneously. This monovalent vaccine obtained in the standard 5 ml commercial packaging is to be differentiated from two other lots of monovalent vaccine which had been made available to U S Naval Medical Research Unit No 4 for experimental study by two other manufacturers.<sup>3</sup>

Because a polyvalent vaccine had again been planned for use in the fall of 1957 and contracted for in March of 1957 it was necessary to renegotiate the contract and substitute an Asian strain in the formula. The final formula of this aqueous polyvalent vaccine included 200 CCA units each of the Swine PR301 FM1 Japan/305 strains of influenza A viruses and the Great Lakes 1954 strain of influenza B virus per ml. This vaccine which became available for use throughout the Navy about 1 October is hereafter referred to as 1957 polyvalent.

The 1957 polyvalent vaccine was distributed for use mostly at shore installations and in the Pacific Fleet. Operational units were instructed to use a dose of 1 ml subcutaneously but non operational personnel and dependents were to receive it intracutaneously. Where used military personnel received two 0.1 ml intracutaneous injections at different sites simultaneously dependents only a single 0.1 ml injection.

Data from sources other than the U. S. Naval Medical Research Unit No. 4 cited in the text have been abstracted from the routine message and written special epidemiologic summaries forwarded to the Bureau of Medicine and Surgery, Department of the Navy, by ships and stations upon occurrence of unusual outbreaks of infectious diseases.

#### OBSERVATIONS

##### Monovalent 200 CCA Asi Str n Influenza Vaccine

The previously mentioned monovalent Asian strain vaccine consisted of a single lot from one manufacturer. It was distributed in late August to over 200 ships, most of which were at East Coast ports preparing to depart for the NATO exercises. Ninety of these ships made special message reports of outbreaks of Asian influenza at sometime between July 1957 and January 1958. Fifteen outbreaks have been serologically confirmed as to the causative virus. On 41 ships the onset of the outbreak was 10 or more days after the crews were vaccinated and the cause was confirmed serologically on 9 of them. On 20 ships outbreaks had terminated prior to vaccination of the crews and three of these were confirmed serologically. In 26 other outbreaks the relationships between the beginning of the outbreak and vaccination date could not be defined exactly or vaccination was begun during or just before the outbreak. Not all of these 90 ships submitted a final written epidemiologic summary giving exact data on personnel strength, total cases, and other details during the period of the outbreak. The attack rates on ships reporting only by message were essentially similar to those submitting both messages and final written reports but only the latter were utilized in the subsequent analyses.

The fact that 101 ships did not make a special message or written report of influenza was of no significance because it was known that many ships failed to make such reports during

the period in which influenza was widespread. Many of the ships that failed to submit messages could be identified as having experienced epidemics through regular morbidity reports, other ships having named them as contacts, and positive serologic reports from laboratories. Incompleteness of data precluded their further consideration.

In table 1 are summarized data on the attack rates during outbreaks of influenza which had subsided prior to or which began 10 or more days after vaccination. Summaries from all ships included claimed that all personnel, with the exception of an occasional individual sensitive to eggs, were vaccinated with 1 ml of the monovalent vaccine subcutaneously.

TABLE 1. Attack rates of influenza on ships

Classification of ship	Number of personnel	Total exposed	Total	Attack rates			
				Epidemic		Epidemic	
				Attack rate	Range	Average	Range
Destroyer	1	2,340	748	31.9			
Destroyer	1	3,495	631	18.1			
Cruiser	1	1,505	355	23.6			
Destroyers	6	1,465	653	44.5	15.3-60.6		
Oiler	4	644	1,014	38.3	15.3-48.0		
Total	13	11,449	3,401	29.7	15.3-60.6		
Destroyer	1	1,534	489			31.7	
Destroyer	3	8,624	2,462			28.6	2.6-30.9
Cruiser	2	3,105	8.9			26.6	2.6-29.9
Destroyer	19	4,448	1,651			3.3	12.2-62.3
Oiler	9	3,324	1.06			31.9	8.7-64.7
Total	34	21,035	6,493			30.7	8.7-64.7

Only those ships in which the attack rate was 10% or more are included. The attack rate is based on the number of personnel exposed to the vaccine.

From this tabulation it seems clear that while there was considerable variation in attack rates between ships this was unrelated to whether or not the crews had received the monovalent Asian strain influenza vaccine. The attack rates in the aggregate personnel were remarkably similar despite this variation in individual units. It was also evident from the reports that no major modification of illness occurred, as judged by the range of fever, duration of illness, or variety of symptoms, in those who developed influenza before and after a vaccination program. Attack rates and clinical descriptions of the disease reported from ships where vaccination was begun during epidemics or at some unspecified time in relation to it were consistent with the experience of either group of ships in table 1.

A few specific instances are cited as examples of these shipboard outbreaks occurring 10 or more days after vaccination with the monovalent influenza vaccine. The entire crew of a submarine received 1 ml of the vaccine subcutaneously on 3 October. An outbreak began on 20 October, a few days after tying up along

side a sister submarine on which influenza was occurring. Sixty per cent of the crew became ill in the next 10 days many with fever to 103 to 105 F. The outbreak on the sister submarine began on 14 October and involved 65 per cent of her crew. Influenza vaccine was not administered on this submarine until 17 October. The crew of a fast attack transport were given 1 ml of the monovalent vaccine on 27 August and 1 ml of the 1956 polyvalent vaccine on 30 September. An outbreak involving 69 per cent of her crew began on 6 October while at Taranto Italy. Four of five pairs of sera submitted from this ship to a Navy Preventive Medicine Unit exhibited diagnostic Asian strain antibody titer rises. A final example is that of an aircraft carrier whose crew was vaccinated subcutaneously with the monovalent vaccine on 3 September. During the next 11 days the ship was at sea. On 20 September six days after arrival in Scotland an influenza outbreak began in which 31 per cent of her crew were involved by 15 October. Diagnostic increases in Asian strain antibodies occurred in five of six pairs of sera submitted to a Navy Preventive Medicine Unit.

The first or acute sera of previously vaccinated patients from these ships which were submitted to laboratories for diagnostic studies were devoid of antibodies against the Asian strain at the lowest dilutions used in the tests. This coincided with the results of antigenicity studies carried out at Great Lakes (table 2). Neither did controlled studies at Great Lakes using this commercial monovalent vaccine exhibit any evidence of significant protection.

Reports of influenza outbreaks occurring between April and August 1957 were received from 16 other ships including destroyers a cruiser and aircraft carriers. All of these ships were operating in the Pacific at the time of these outbreaks except for two destroyers which were at Newport R I. The attack rates reported ranged from 13.8 to 66.3 per cent on individual ships with an average of about 30 per cent.

These data indicate that the experience of those ships which received monovalent vaccine was consistent with that of ships which became involved before the vaccine was available. The vagaries of spread of the disease among personnel of ships which accounts for the variation in attack rates cannot be explained other than to state that the variation appears to be real and not entirely due to differences in diagnostic criteria or reporting. Several ships have reported more than one outbreak and one (to be described later in this article) had two separate confirmed outbreaks. Such variation however points to the difficulties in evaluation of prophylactic measures within a small group of ships and offsets many of the individual opinions which were expressed pro or con by individual commands about the effectiveness of the vaccine on the basis of comparison with other ships in the vicinity.

TABLE 2 Hemagglutination inhibition antibody titers to influenza viruses in adult persons  
October to December 1957

Vaccine	Dose	Number of subjects	A/J P /305/57		A/Great Lakes /1148/53		B/Great Lakes/176054	
			Percent with titers	Geometric mean	Percent with titers	Geometric mean	Percent with titers	Geometric mean
			>10	>20	>10	>20	>10	>20
1956-poly let	1.0 ml subcutaneously	12	(0) 8	(0) 0	(50) 67	(10) 33.5	(100) 100	(21.5) 100.0
1957-poly lent	1.0 ml subcutaneously	65	(11) 28	(3) 20	(39) 49	(12.4) 16.3	(55) 57	(28.5) 35.0
1957-mono lent	1.0 ml subcutaneously	35	(3) 9	(0) 6	(21) 31	(<10) 16.5	(38) 40	(36.3) 51.0
1957-poly lent	0.2 ml intracutaneously	42	(24) 43	(7) 31	(21) 31	(<10) 10	(38) 40	(36.3) 51.0
1957-mono lent	0.2 ml intracutaneously	37	(0) 5	(0) 3	(21) 31	(<10) 10	(38) 40	(36.3) 51.0

Percentages = per vaccinated  
No. in parentheses = per total  
(141 or 303)



### Shipboard Experience With the 1957 Polyvalent Vaccine

Due to the late distribution of this vaccine and the fact that most ships in the Atlantic Fleet received the monovalent vaccine relatively few instances were reported where it could be ascertained that this vaccine had been given 10 or more days prior to beginning of an outbreak.

Four destroyer type ships submitted final epidemiologic summaries indicating outbreaks had begun 10 to 30 days after the crews were vaccinated with 1 ml subcutaneously. There were 256 cases among the total of 793 men on these four ships. The total attack rate was 32.3 per cent with variation on individual ships from 15.3 to 54.2 per cent.

An attack transport reported an epidemic during a cruise to Alaska in October in company with a sister transport. The attack rate on the reporting transport personnel of which were unvaccinated was 36.2 per cent. On the sister transport personnel of which had been vaccinated 7 to 10 days prior to beginning of the outbreak the attack rate was 32.6 per cent. The report concluded. On the basis of this limited study there appears to be no significant decline in incidence between inoculated protected (ship) and control (ship).

A destroyer escort reported immunization of its crew of 151 men on 25 September with 1 ml of 1957 polyvalent vaccine subcutaneously. Epidemic influenza began on 24 October. A total of 81 cases occurred an attack rate of 53.6 per cent. This outbreak was not confirmed as to cause but occurred while the ship was alongside another in which a confirmed outbreak was occurring. Another destroyer escort reported an attack rate of 54.2 per cent in the crew which had been vaccinated subcutaneously 10 days prior to the beginning of an outbreak. In contrast two destroyers with outbreaks beginning 14 or more days postvaccination reported attack rates of 15.3 and 20.6 per cent and a cruiser reported only 9.8 per cent of its crew involved. There were no notable differences in the clinical description of disease occurring aboard these ships from those of unvaccinated ships and the only conclusion that can be reached is that the disease did occur in high incidence and without major modification of severity among personnel vaccinated 10 or more days before the beginning of outbreaks.

Interpretation of additional reports was complicated by the possibility that ships were undergoing a second outbreak of influenza rather than initial outbreaks during the postvaccination period. U S Naval Medical Research Unit No. 2 investigated an outbreak occurring in a destroyer division in the Philippines during November and December. Men on the four destroyers involved had received 1957 polyvalent vaccine between 17 and 29 October and the 1956 polyvalent vaccine in August of 1957. Each of the ships had experienced an outbreak of influenza like illness during June and July of 1957 while operating in the

Long Beach, Calif area In November, one destroyer had an attack rate of 49.5 per cent despite the possibility that some personnel previously had had the disease and that both 1956 and 1957 polyvalent vaccine had been administered in the three month period prior to the beginning of the second outbreak. The destroyer on which the fewest cases had occurred at the time of the investigation had experienced the highest attack rate (approximately 15 per cent) during the July outbreaks.

Of interest in this regard was the report from an aircraft carrier in the Pacific. Between 1 and 18 July, while operating in the San Diego, Calif area, an outbreak of influenza like illness occurred with 227 cases, or an attack rate of 10.4 per cent. Of the 227 cases 157 (69 per cent) were admitted to sick bay. The distribution of maximum oral temperatures in these 157 cases is shown in table 3. The average duration of illness was 3 days.

TABLE 3. *Distribution of maximum oral temperatures in hospitalized patients during two confirmed outbreaks of Asian influenza on same aircraft carrier*

Maximum oral (F) temperature	Patients with elevated temperatures			
	First outbreak (July)		Second outbreak (November)	
	Number	Percent	Number	Percent
104	14	8.9	20	11.0
103	38	24.2	43	23.7
102	63	40.1	78	43.1
101	24	15.3	27	14.9
100	12	7.6	11	6.1
99	4	2.6	1	0.6
98	2	1.3	1	0.6
Total	157	100.0	181	100.0

All men admitted had received the 1956 polyvalent vaccine during the preceding winter. A second epidemic occurred on this carrier between 1 and 27 November while it was operating around Japan with a total of 447 cases, or an attack rate of 16 per cent. Of the 447 cases, 181 (41 per cent) were admitted and the distribution of oral temperatures in these 181 men is also shown in table 3. The average duration of illness was 4 days.

The 1956 polyvalent vaccine had been administered to the crew of this carrier between 20 and 25 August. The 1957 polyvalent vaccine was given on 14 and 15 October. The latter vaccine was given intracutaneously, each man receiving 0.1 ml in the volar surface of each forearm, a total of 0.2 ml. On the basis of the higher attack rate and clinical similarity of patients ad-

mitted during the two epidemics medical officers were of the opinion that the two doses of polyvalent vaccine one of which contained 200 CCA units of Asian influenza virus had been ineffective in preventing or ameliorating the disease. No comment was made in the epidemiologic reports from the ship as to the lesser percentage of total cases admitted during the second outbreak. This could have been a reflection of milder disease or simply exhaustion of hospitalization facilities due to the greater number of cases. Three pairs of sera collected from patients ill in July were reported by the Sixth Army Medical Laboratory as showing diagnostic rises in antibody titer for the Asian strain. Asian strains of influenza were isolated from 9 of 11 throat washings collected by a team from U S Naval Medical Research Unit No. 2 during an epidemiologic study of the November outbreak. Diagnostic antibody rises occurred in 30 of 36 pairs of sera. Only one man of those with acute tonsillitis during the November outbreak had been ill in July. These observations suggest that illness during the July outbreak conferred relatively complete protection in November.

#### Results of Controlled Study on Effectiveness of Vaccine at the U S Naval Training Center Great Lakes

Figure 1 shows the reported febrile respiratory disease rates in naval recruits at Great Lakes two or more weeks after subcutaneous and intracutaneous inoculation with either a placebo solution or the commercial monovalent Asian influenza vaccine. During the period of these studies Asian influenza was diagnosed in 14 to 89 per cent of hospitalized cases tested by serologic methods or virus isolation techniques. The intracutaneously inoculated group experienced an average reported illness rate of 63.4 per 1,000 per week during the study period as compared to 84.3 per 1,000 per week in its placebo control group. The illness rate in the subcutaneously vaccinated group was 54.9 per 1,000 per week as compared to 59.4 per 1,000 per week for its control. The maximum illness rates occurred somewhat later in the vaccinated men than in the control groups which suggests that the use of this vaccine may have modified the behavior of influenza in these groups. Undoubtedly the slight degree of protection observed would be detected only under controlled conditions.

In contrast to the poor results observed with the monovalent vaccine distributed to naval activities in the Atlantic and Mediterranean areas are those obtained using a monovalent Asian strain vaccine prepared by another manufacturer. This latter vaccine contained 200 CCA units of A/Japan/305/57 strain per ml and was administered subcutaneously in a 1 ml dose. Summary results of this study, the details of which were reported elsewhere, are shown in figure 2. The reported febrile respiratory disease rates in naval recruits inoculated with either the experimental Asian vaccine, the 1956 polyvalent vaccine, or a control

solution, are shown for each week of the study period. It is apparent that a marked reduction in reported respiratory illness was associated with the use of this monovalent vaccine. The 1956 polyvalent vaccine failed to prevent an outbreak of respi

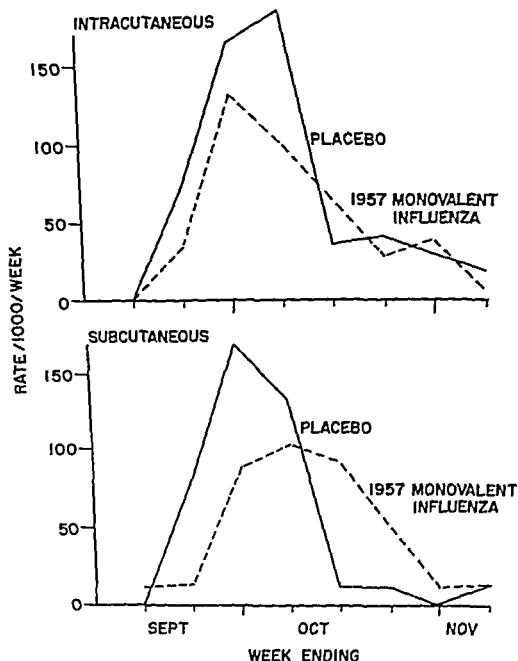


Figure 1. Reported respiratory disease rates per 1000 per week for placebo and 1957 monovalent influenza vaccine groups in the intracutaneous and subcutaneous routes of administration.

respiratory disease in the population in which it was used. However, the slight, but statistically significant, reduction in illness rates in this group is of considerable interest in connection with the immunology of influenza.

# Results of Human Antigenicity Studies with Several Vaccines Used in the Navy

The antibody response to vaccination with the vaccines used at Great Lakes and with the commercial vaccines was examined by the U S Naval Medical Research Unit No 4 Table 4 shows the results of these tests in naval recruits It appears that the protamine precipitated vaccine (vaccine A) was the most potent antigenically in terms of the percentage of men responding with

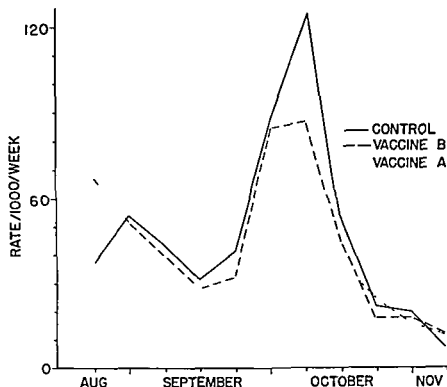


Figure 2 Report of febrile prodromal attack at onset and control of influenza in two or more weeks after natural vaccination. A = monovalent vaccine with protamine precipitated B = 1956-57 lyophilized influenza (R produced with p m f m N w E g l d j l f M d N mb 20 1958)

antibody titer levels of 10 to 20 or greater and in terms of the mean titer of the group after subcutaneous vaccination as compared to the results in its placebo group Of interest here are the results using vaccines B and C Forty five per cent of the men receiving vaccine B had antibody titers of 20 or greater two weeks after subcutaneous vaccination while none in their placebo counterpart had antibody titers of this magnitude The data indicate that vaccine C the vaccine issued to naval units in the Atlantic and Mediterranean areas was a comparatively poor antigen when given either subcutaneously or intracutaneously The effectiveness of vaccines B and C in the prevention

of acute respiratory disease was investigated in field trials at Great Lakes As stated above, only slight clinical protection was observed in association with the use of vaccine C Vaccine B, on the other hand, was highly efficacious in reducing acute febrile respiratory illness rates Thus, prophylactic efficacy of these vaccines correlated well with their antigenic potency with respect to the epidemic viral strain Unfortunately, no observations on the efficacy of vaccine A are available because the population in which it was being studied was no longer under observation during the period of influenza prevalence at Great Lakes

TABLE 4 A t body p t m lent A an t fl l ly t S pt mb 1957

V	D d	V d			C l		
		Numb f ubj	P w h		N mb f ubj	P w h	
			<10	≥20		≥10	≥20
A	10 ml ub-ly	19	84	79	40 0	10	20
B	10 ml b-ly	33	61	45	14 2	31	3
C	10 ml ub-ly	27	33	14	<10		
	01 ml ut ne usly	50	18	8	<10	21	5
	02 ml ly	25	48	20	<10		

R p oc l b g i n on h b an body A/J pa /305/57  
V us A P tamia p p r ad in 500 CCA un pe ml  
B Aque us 200 CCA un pe ml  
V C A ue us 00 CCA un p ml V used by val un A I ed Med ranean

Serum specimens were obtained by several Navy Preventive Medicine Units from men stationed at shore stations and aboard ships in the Pacific, Atlantic, and Continental United States areas, before and after inoculation with influenza vaccines procured from commercial sources by the Navy These specimens were tested for influenza hemagglutination inhibition antibodies by U S Naval Medical Research Unit No 4 Table 2 shows the results of these tests The antibody titer response to the 1956 polyvalent vaccine, which did not contain Asian influenza antigen, was significant to an A prime and a B influenza antigen As might be expected, no titer response to an Asian strain antigen was observed with this vaccine The antibody titer response to the 1957 polyvalent and monovalent vaccines was uniformly poor, even to A prime and B influenza antigens also contained in the polyvalent vaccine, and with which these men presumably had had prior experience The data suggest, however, that the 1957 polyvalent vaccine may have produced a better Asian strain antibody response than did the monovalent vaccine These results suggest that the vaccines in use by the Navy in the fall of 1957 were relatively impotent antigenically The results of the con

trolled study with one lot of these vaccines at Great Lakes support this conclusion

### DISCUSSION

Several reports have appeared which establish beyond question that a 1 ml dose of aqueous vaccine containing about 200 CCA units of an Asian strain of influenza virus will reduce respiratory illness morbidity during epidemics of Asian influenza.<sup>1</sup> With one exception these reports have been preliminary and based on the incidence of gross acute respiratory illness. Variation in apparent degree of protection between the several studies is as yet unassessable because this will depend on the Asian influenza specific attack rates in the experimental populations. In the one study in which such rates have been measured human volunteers were experimentally infected and the comparability of results to what might be expected in naturally occurring disease is unknown.

The controlled studies by U S Naval Medical Research Unit No 4 among recruits at Great Lakes using a commercially prepared vaccine have also shown reduction in total acute respiratory illness during an epidemic of Asian influenza. In contrast the somewhat limited trial of monovalent vaccine prepared by another manufacturer obtained through normal military procurement channels provided no such reduction. From the data presented herein it seems clear that this same monovalent vaccine was virtually worthless from the standpoint of any significant degree of protection or modification of illness when used in the personnel of ships. The same assessment would also seem to apply to the 1957 polyvalent vaccine containing the Asian strain which was a product of the same manufacturer. While there was some suggestion that reduction in the incidence of illness followed use of the 1956 polyvalent vaccine it was at most very minor and of no practical significance.

The Commission on Influenza of the Armed Forces Epidemiological Board has described the difficulties encountered by the manufacturers in producing a vaccine of the desired potency and in the assay of potency by the usual methods. They have also interpreted the results of controlled studies on antigenicity and effectiveness of the early products as indicating that vaccines assayed as containing 200 CCA units of Asian strain influenza viruses were suboptimal. In view of this basic inadequacy of the vaccine and the technical difficulties surrounding its manufacture and potency testing, it is not surprising that one or more lots of vaccine should be of such low potency as to be essentially valueless. The open question is to what extent this occurred and how many other groups shared the Navy experience with commercially released lots of vaccine? Even if it should be ascertained that the Navy experience was unique there would seem to be a clear indication that more research on methods of production and assay is needed and that field testing should include vaccines procured for general use. Normal

governmental procurement procedures require competitive bidding and acceptance of the lowest bid(s). This in itself will require the successful bidder to shave production costs to a minimum. At present, there is grave doubt as to the abilities of either the producer or receiver to assay the probable protective value of the vaccine with any high degree of accuracy, on the basis of a chicken erythrocyte agglutination test.

There seems to be a direct relationship between the ability of vaccines to stimulate antibodies against the Asian strain in humans and the protective efficacy of the vaccine. In human volunteer studies, Bell and co-workers found some degree of correlation between the antibody titers and the development of febrile illnesses following inoculation with Asian influenza viruses. The relatively good antibody response in Navy recruits from vaccines providing protection is sharply contrasted to the weak responses following vaccines that provided little, if any, protection. Antibody rises following infection have generally exceeded by a considerable degree those following any of the 200 CCA unit vaccines, and there appears to be relatively solid immunity for at least several months following the natural infection. Vaccination with the older polyvalent vaccines did not stimulate measurable antibody against the Asian strain. While there might have been a little protection conferred by this vaccine, if the experience among recruits is not to be written off as a chance variation, it was so slight as to have no more than academic significance.

The failure to obtain definitive information on the comparative protection afforded by intracutaneous and subcutaneous administration of the vaccines was disappointing. The poor antigenicity of the available vaccines and failure of protection with the subcutaneous route, would have precluded comparisons, even had it been possible to obtain and distribute vaccine at an earlier date. Because of the importance of this question, when decisions must be made in utilization of inadequate supplies of vaccines to meet requirements by the usual dosage, more information is necessary. It was surprising to encounter such conflict in opinions and so little definitive data at the time decisions had to be made in the early fall of 1957.

This partial summary of the Navy's experience with Asian influenza and specific vaccines against these strains of influenza viruses has emphasized both the military need for an effective vaccine and the inability of the vaccine procured through normal procurement channels in the early fall of 1957 to meet this need. Undoubtedly, the later vaccine would have provided a higher degree of protection but the delay in their availability was far too long for military purpose. When the next new variant appears, if critical operational units vital to the military defense of the country are still scattered throughout the world, some quicker way must be found to provide effective protection, if defense is not again to be jeopardized. If a unit are involved



as the disease passes through the country in which they are located and there is little time available between first appearance of the variant and the involvement of critical military populations

### SUMMARY

Epidemics of Asian influenza occurred on Navy ships and stations as the disease spread from the Far East around the world. This afforded records of outbreaks in relatively comparable populations before and after the initiation of vaccine programs in the early fall of 1957. In addition controlled studies with several vaccines were conducted among recruit volunteers at the U S Naval Training Center Great Lakes Ill.

Monovalent vaccines containing 200 CCA units of Asian strain influenza virus per ml prepared by two different manufacturers were tested by U S Naval Medical Research Unit No. 4 at Great Lakes. One of these was highly effective in reducing attack rates for febrile respiratory illness during an epidemic of Asian influenza the other was not effective. The same monovalent vaccine from the third manufacturer did not appear to provide any significant protection from or modification of illness caused by Asian influenza viruses when used routinely in personnel of ships of the Atlantic Fleet.

Reimmunization with older polyvalent vaccines not containing Asian influenza virus which had been used routinely during the winter of 1956-1957 did not provide any practical reduction in attack rates for Asian influenza. Major outbreaks also occurred in personnel who had been immunized by either the subcutaneous or intracutaneous routes with a new polyvalent vaccine containing 200 CCA units of Asian strain of influenza virus. The ability of vaccines to stimulate significant increases in hemagglutination inhibiting antibodies in man was correlated with their protective ability. Some evidence was obtained which indicated that a relatively solid immunity persists for at least four months following illness with Asian influenza.

The experience has emphasized the need for further research on methods for production and assay of vaccines containing new variants of influenza viruses if adequate protection of military forces throughout the world is to be envisaged when the next major variant appears.

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### THE NEED FOR MEDICAL STATESMANSHIP

Do we still believe in better standards of medical education and medicine or are our ideals changing and does a commercial economy occupy an increasingly prominent place in medical ethics? Are we protecting mediocrity? Nor is it medicine only that faces this issue today but also the dental branch of the healing arts. We are at a parting of the ways—one points toward true statesmanship the second toward defense of the weaker elements and continued defense of procedures and methods that worked well 30 and 40 years ago but now need readjustments or revitalization if you will along with the changing picture of our general economy. In my opinion this second road the vigorous defense of the status quo ante encourages the development of socialized medicine and dentistry in spite of its protagonists who themselves may fear the role of true statesmanship in our profession. Quite the contrary if we wish to prevent such socialization then we must all face the question squarely exert leadership and promote cooperation between our profession and local State and Federal governments. If there is continued resistance with hesitancy to lead and develop plans we shall surely be overwhelmed.—Frank B. Berry Problems Confronting Medicine Today *Virginia Medical Monthly* October 1958

# TREATMENT OF ACUTELY COMPRESSED VERTEBRAL BODY BY IMMEDIATE PROGRESSIVE MOBILIZATION

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JAMES J SCHUBERT *C pt USAF (MC)*

**C**OMPRESSION of the thoracic and lumbar vertebrae is the result of sudden flexion from acute trauma or stress. It is a common injury especially in the aged female. This injury in the aged usually is caused by minimal trauma or stress, the osteoporotic bone being susceptible to damage. In the young, however, the fracture usually is associated with more severe trauma especially when resulting from automobile accidents or falls from significant heights. All patients complain of local vertebral tenderness and generalized paraspinal myalgia. There may be a transitory abdominal distention or urinary retention.

Since the advent of radiographic control in fracture reduction, there has been rather uniform agreement in the management of these injuries. Precise reduction and prolonged immobilization in hyperextension until consolidation in anatomic position occurred were insisted on by Davis, Böhler, Watson, Jones, and Rogers. Minor variations of treatment have been advocated but generally they all fall into the same method.

This article is not addressed to those who are following the teachings of these masters who are anatomically reducing the fractured vertebrae and maintaining the reduction by continuous immobilization until the fracture has consolidated in anatomic position. We do not wish to take any position in regard to the necessity of precise reduction or the feasibility of maintaining it, although the following paragraphs will indicate that patients do quite well without reduction.

This article does deal with the relative merits of the prevalent method of treatment of the fractured spine which seems to have evolved in practice without particularly following the principles established by the above mentioned authors, which form of treatment consists of the application of a body cast using one of the commercial devices designed for the application of a

hyperextension cast " Roentgenographic casts reveal that the original position had not been changed substantially. The maintained for a variable period of time was considerably short of the period of immobilization guarantee consolidation after reduction followed by some form of brace to be worn which the physician considers adequate of that management are satisfactory in cases so treated

A residual group of patients however degree of complaints which fall into the somatosomatic sphere. Somatic findings roentgenographic examination and reveal corbrae in exactly the same position as a and which had been maintained in a plus variable findings such as degeneration both the adjoining disk spaces and attempt toward body fusion by calcification ligaments. Functional results however patients character and behavior pursue conquer the world as athletes or other their professional fields will have. Persons who are insecure or lacking the challenge of life may revert to partial or total support. The complaint individual for unless they themselves justification of their claims, they could society to offer its breast. There is still that the incidence of somatosomatic is proportion to the duration of the main fracture. The current study pertains to the long the period of treatment of the fracture of exposure and incidence of somatosomatic

In recent years Nicoll in England series of patients in which no attempt and no immobilization was used. His results with those of hyperextension and immobilization obvious advantages. Not only did the comfortable method of treatment but was and employment much sooner. In a neuroses of the painful and weak back condition and insurance claims were greatly

Also in the literature many refer that even after reduction with hyperextension immobilization in plaster the majority on roentgenographic examination less time of the original injury.<sup>6</sup> Hence advantage of simple bed rest should be investigated

## MATERIAL

During the period 1953-1957 a total of 35 patients were hospitalized because of isolated acute compression fractures of the thoracic and lumbar vertebrae. The patients fell into two major treatment groups. One group consisted of 12 patients whose initial treatment was begun elsewhere and by hyperextension body casts. These patients were seen at Letterman Army Hospital for follow up care only. The second group was comprised of 23 patients who were treated primarily at this hospital. All patients in this second group were treated with immediate progressive mobilization. Patients with associated fractures of the long bones are not included unless the associated fractures or injuries did not affect our method of treatment. Likewise patients on ancillary services who were seen on consultation were not included due to lack of control. Our series did not include those with compression fractures resulting from osteoporosis or electroshock therapy.

## METHOD

The concept of immediate mobilization in major injuries of the extremities has long been advocated and practiced by the senior author. The relief of pain in the injured extremity by immediate motion is thought to be due to a specific action of active motion in decreasing inflammatory reaction. During the period of 1953-1957 this concept was applied to all patients suffering acute compression fractures of the thoracic and lumbar spine who were treated under the direct supervision of the orthopedic service. In this rapid treatment program we are guided by two observations. First that fractures not only affect the immediate weight bearing function of the injured bone but simultaneously produce a physiologic interference with the muscle function of the affected area. Initial measures therefore were aimed at immediate rehabilitation of muscle function which is carried out with the patient at strict bed rest and by practicing rolling over from one side to another. This usually can be accomplished within the first two days and successful return of muscle function is announced by disappearance of pain. Second pain is considered a part of an over all inflammatory reaction and is respected in the same sense as the flashing red light at the railroad crossing. The recurrence of pain after normal muscle function has returned indicates that the fracture has been subjected to undue stress. Future progress of the patient therefore is regulated on the basis of permitting any function which can be carried out without eliciting pain. It is quite revealing that ambulation at first in limited periods and distances can thus be resumed within a few days after injury. We have found however that tolerance for prolonged sitting or standing is much slower to return and should be restricted during the early weeks of convalescence. Following the injury the patient is told that he has to regulate carefully his activities in that respect. We

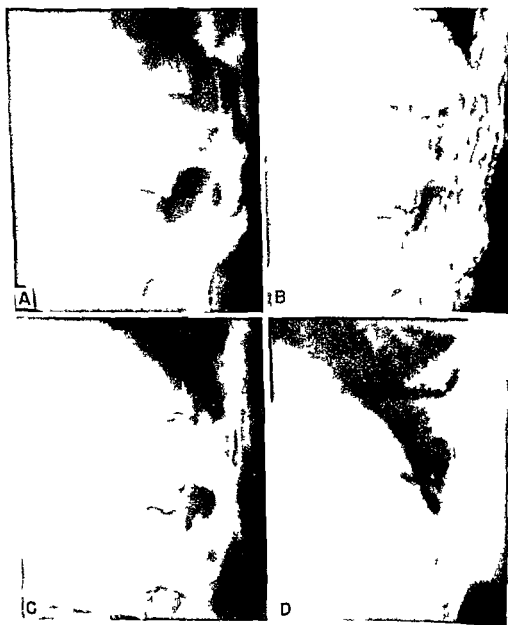


Fig e 1 (A) Appea anc of / st lumba v t b a at time of injury (B) Rrent  
 genog am made through plast r type xt ns on jacket 40 days after injury  
 (C) Roe tg nogram mad 90 days afte inj ry Back brace was used /  
 xt four months (D) Six month afte injury Total tr atme t 90 days is  
 body cast 120 days t brace

have found that ambulation and exercise can be carried out with impunity if these criteria are kept in mind

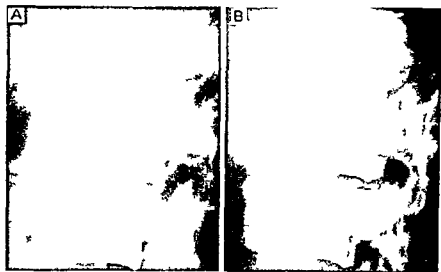
### RESULTS

Results are tabulated in table 1 The average number of days at absolute bed rest was 10 while total days of hospitalization averaged 18 This time frequently included administrative processing following completion of treatment In civilian practice

TABLE 1 Duration of treatment of patient with hyperextended elbow fracture

Treatment	Number of patients	Average (years)	Average time (days)			Total treatment time (days)
			In	In b	A b d	
Hyperflexion	12	26	57	120		177
Immediate mobilization	23	41			10	18

total hospitalization would more closely approximate bed rest time In the 12 patients seen who had been treated with hyperextension body cast the average time in plaster was 57 days



Figur 2 Roentgenogram showing (A) appearance of elbow at time of injury and (B) 60 day later. Patient with body cast for 60 days

In addition 10 more days were required on the average to properly mobilize the patient and rehabilitate him sufficiently to return to duty Patients treated with progressive immediate mobilization returned to duty on the average of 18 days following injury All were free of pain with a normal range of motion A

restricted profile preventing any undue stress was given patients for varying periods of time three to six months



Fig 3 Roentgenograms (A) at time of injury (fracture) and (B) 60 days after injury when patient was asymptomatic.

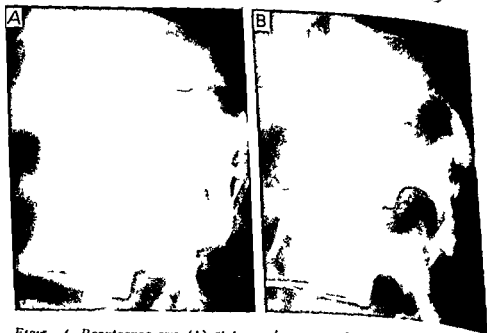


Figure 4 Roentgenograms (A) at time of injury and (B) 90 days after injury when patient was asymptomatic. The total time spent in bed was 14 days.

In many instances follow up in our series was not possible because of changes in military assignments. However, some were followed for periods up to two years. Comparison of the appearance of the wedged vertebrae with both methods



possible. Figures 1 through 6 are representative of each. It is apparent that reduction accomplished by hyperextension frequently is lost with the immobilization technique. In most cases

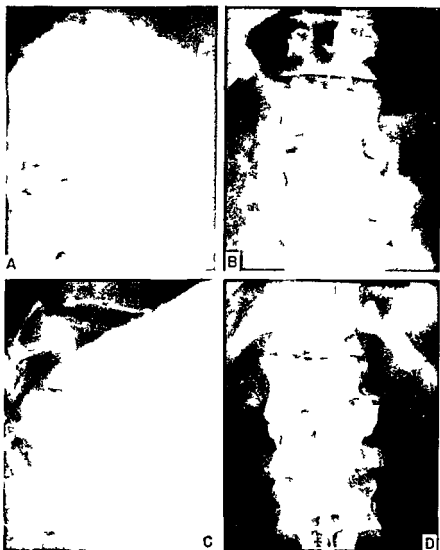


Figure 5 (A) and (B) App a a t t m f j j y w t h t t m t b y m m d i a t m b i l i t o n (C) and (D) T u y j l l w g j r y N o r m a l j t

reduction was not made at all but the patient was continued in a hyperextension cast. In those cases treated by immediate progressive mobilization, no great change in appearance of the fracture was noted. Anterior compression was not increased.

## COMPLICATIONS

Each case was studied for untoward complications. No patient treated by immediate mobilization developed neuropathy during treatment. One patient developed a cord bladder six months following his injury and was subsequently found at laminectomy to have an arachnoid scar. It was believed that this probably was not related to treatment, but due to the original trauma.



Figure 6 Appearance of patient and range of motion attained following treatment

## SUMMARY

The established teachings of the past masters of orthopedic surgery in the management of compression fractures of vertebrae remain unchallenged. In prevalent practice these fractures are treated for varying periods of time in hyperextension casts and back braces without reduction. Although the over all results are good, significant residual complaints of a sociosomatic nature occur. Such complaints from back injuries are believed to arise in direct relationship to the length of time of treatment. A method of treatment and our results in which the time factor is substantially reduced and where functional results are excellent are presented.

was a psychiatrist. The sampling was random for, in our sick call the patients were assigned to the physicians by the corpsmen who picked up the charts and called out the name of the patient without first seeing him thereby eliminating a conscious or unconscious selection on the part of the corpsmen. The following routine was followed with each patient. Past and family history was obtained and then by use of the associative anamnesis data were collected as to the nature and severity of any symptoms of anxiety a character and behavior disorder or emotional factors which had prompted the patient to come to the physician. At the end of the interview the examiner directly inquired as to the presence of symptoms of anxiety not mentioned. The patient was then classified as follows:

A Anxiety scale and/or chronic

- |            |  |
|------------|--|
| 0 Non      | No appreciable anxiety   |
| 1 Mild     | Very mild symptoms of anxiety  |
| 2 Moderate | Symptoms of sufficient severity to cause the patient frequent and acute distress in almost all situations inhibiting working performance   |
| 3 Severe   | Symptoms of such severity that the patient was at times unable to function. These were the patients who had histories of panic hyperventilation very low frustration tolerances etc. |

B Presence of a character and behavior disorder

- |   |  |
|---|--|
| 0 | None noted   |
| 1 | Very occasional and mild episodes of outbursts   |
| 2 | To such a degree that the relationship with other and their superiors were threatened                                  |
| 3 | These were patients with a history of one or more company punishment courts martial demotions for disciplinary reasons |

C Opinion of the examiner as to the emotional factors prompting the sick call visit

- |   |   |
|---|---|
| 0 | No apparent   |
| 1 | Slight suggestion   |
| 2 | Moderate evidence   |
| 3 | No organic illness found and the patient presented primary psychiatric syndrome |

The patient's record was then reviewed it was noted how long he had been in Alaska and the number of months remaining prior

to leaving The number of visits to sick call per three month time interval was noted Return visits at the suggestion of the physician were not included Thus, only visits of the patient's own volition were counted (fig 1)

## MEDICAL SURVEY FORM

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L w b k p ( l g ) Phy al am an f l m ar g  
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Ar h b NP ? ( laborat f y )  
P h J ur l on in in h rv  
1) Su d g ur  
2) In d dr k g in g m ar  
3) D pl ry d mot  
4) D ft ul y h gh hool ; ed USAF

DEGREE OF ACTING OUT SEVERE CLASS 3

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Y p lp on westing palm h rt f b arch l in an f l  
en Symptom h been pe en f w y at A ur in in ympt m ar  
om g m f q ly

ANXIETY ACUTE AND CHRONIC MODERATE SEVERITY CLASS 2

I h ur f an ld ll ( f pl )  
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rt b l pau

M h ll

F gu 1

A request was then sent to the patient's organization for the name of a man of similar age, race, rank, and level of education. This person's record was pulled from the hospital files and data as to the number of visits to sick call per three month period were recorded. In addition, the number of months remaining prior to leaving this overseas station and months served were noted. In this way a control group was obtained which indicated the average number of visits per unit time and influence of time spent in the area on sick call attendance. This group is considered to be a random sample of the organizations from which the patients came. In the strictest sense, this random sample

is not a *control* group nor is the other truly an experimental group. Nevertheless economy of writing and common usage warrant the use of the terms *control* and *experimental*. With the foregoing in mind these terms will henceforth be used. Because the control group was not individually interviewed, it was not possible to classify its members as to anxiety.

### RESULTS

As can be seen from figure 2 there is a marked difference between the group representing a random sample seen in sick call and a control series. It would seem from this graph that a man seen in sick call in general will have nearly twice as many

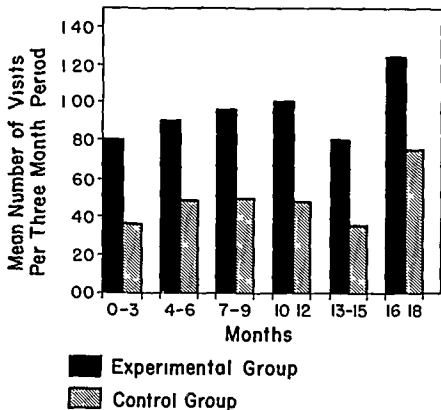


Fig. 2. Comparison of experimental and control groups in sick call attend.

visits as a man in the control series. This is noted during all time intervals. In addition, it is interesting to note that the experimental group had a gradually increasing number of visits to the physician as the tour of duty out of the United States lengthened in time. This is most evident in the 16 to 18 months period. These figures verify the clinical impression that persons who are seen by the physician are not a representative sample of the population, but in fact are a special segment.

Analysis of the data by the chi square method indicates the above difference cannot be ascribed to any significant difference in the number of men present for the various three month periods in the two groups. In addition, the two groups were found to not differ as to the time in the theater at a statistically significant level.

Reviewing the clinical material of the experimental group, it was found that 32 per cent of the patients studied had been given a primary psychiatric diagnosis, whereas, 43 per cent had acute and chronic anxiety considered to be of pathologic proportions, i.e. in the moderate to severe category. Most of these patients were seen not for symptoms of anxiety but for various ills such as upper respiratory infections (table 1).

TABLE 1 Primary psychiatric diagnosis and anxiety in the experimental group (76 patients)

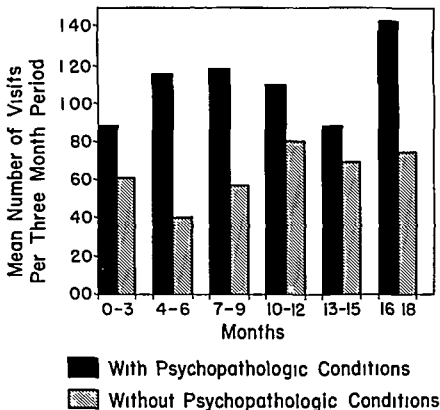
Diagnosis	Number of patient	Percent
Primary psychiatric		
Conversion hysteria	9	
Anxiety reaction	5	
Gastrointestinal reaction	6	
Angioneurotic urticaria	1	
Musculoskeletal reaction	3	
Total	24	32
Anxiety of chronic type and sufficiently severe to be called pathologic		
Moderate anxiety	21	
Severe anxiety	12	
Total	33	43

While the above data indicate a definite difference in the two groups, they in no way "prove" what is responsible for the variations. Inasmuch as it was the examiner's impression that one of the possible factors in sick call attendance might be the degree of psychopathology present, it was decided to break the experimental group into two separate categories. Those patients with moderate to severe anxiety, pathologic acting out, and/or a primary psychiatric diagnosis were compared to those who were not believed to have significant psychopathology. They were compared for three month intervals up to the eighth month. The individuals in the groups beyond that period were not of sufficient number to be meaningful (fig. 2).

It is easily seen that those individuals who were classified as having psychopathologic conditions have a consistently larger number of visits than the group thought to be without significant psychopathology.

## DISCUSSION

The above figures indicate that the sick call population, as a whole differed from the control or randomly selected group. This might mean the patients seen were generally more prone to disease. This of course is a possibility. On the other hand the high rate of psychopathology among the experimental group and more importantly the statistically significant association between psychopathology and the number of visits to the physician suggest many patients are motivated to seek out a physician because of unresolved emotional conflicts. The format may be provided by some relatively minor illness such as a mild upper respiratory infection. This would account for the frequent



Figur 3 Compar f k all t t d f th u th and w th t  
p y b o p t h o l g d t The d t g p h l l y p t d w e r t t d  
t t t l l y t h f l l u g m e r T h m b e r f i t p t h e m t h  
p r i d (f t t l t m t h f g m t) w m p t d f b  
p e r b t h g r p T h f g t h o b t d w h a n d l d u s a

$$t = (x) \sqrt{\frac{n_1 n_2 (x_1 + x_2 - 2)}{(x_1 + x_2) x_1}}$$

The P v l w l t h 0.05 u h h t t t a l l y g f a n t

observation that symptoms are often out of proportion to the illness. In addition, it may explain why many patients consult a physician with an illness of no consequence which past experience should have indicated to them is self limiting. The patient, by attending sick call, might be using his symptoms as a defense against anxiety and, at the same time, making contact with a parental figure in an attempt to assuage his emotional discomfort. An interesting speculation along somewhat different lines is that emotional problems and resultant anxiety may predispose a patient to virus and bacterial infections.

When talking with patients, it was noted that their visits were occasionally cyclical. A person might be seen five times in a three month period and then not again for many months. The associative anamnesis frequently indicated that the patient was undergoing some personally threatening situation at the time the increase in sick call visits was noted.

It was especially interesting to observe those patients whom many nonpsychiatric physicians would have classified as "gold brickers." This term frequently is put forth informally to explain the repetitive sick call visits by some patients. In this study rather than an *explanation* of behavior, this was a *symptom* of a severely disordered personality structure. These patients frequently had anxiety and "acting out" of incapacitating proportions.

One of the original impressions prompting this study was that the sick call group would tend to have an initial increase in visits shortly after arriving in this overseas theater as a concomitant of separation anxiety. These data do not bear this out, but do show a trend toward increasing sick call attendance per three month period with greater time in the area. When visits per unit time are graphed (fig 2) it is found that there is a sharp upsurge in sick call attendance by both the experimental and control groups during the 16 to 18 month period. This might possibly be on the basis of impending reassignment to duty in the United States in 6 to 8 months, i.e. separation anxiety due to expectation. If this were so, one would expect that increased attendance might be present during the succeeding time intervals. As mentioned earlier, the number of men present after 18 months do not allow a definitive answer. Because of the manner of selection of the material climatic conditions cannot be the etiologic factor.

Although this study was made on a military population, the findings may be directly applicable to a civilian practice of medicine. This is partially borne out by the similarity between the incidence of primary psychiatric diagnosis in the Lahey Clinic study,<sup>9</sup> 27.2 per cent, and in this one, 32 per cent.

Furthermore it is important to note that the visit of a patient to a physician is an overdetermined act and as such one is not dealing with a randomly selected individual. This has direct pertinence to the way in which control groups in medical studies are chosen.



For example one frequently sees a control series composed of a group of patients from a hospital ward differing from the one under investigation. In certain projects this may be adequate but data from this study would indicate that in many instances (especially psychiatric research) such a practice could distort data and results due to the automatic bias introduced by using non project involved patients as controls.

## SUMMARY

The frequency of visits to military sick call and the occurrence of psychiatric disorder in 76 consecutive military personnel coming to sick call were studied. The same data were analyzed in a matched group of airmen at the same military base. The military personnel seen in sick call had approximately twice as many visits per unit time as a matched random sample of the base population. When the sick call group was categorized, there was found a statistically significant ( $P = < 0.05$ ) association between psychopathologic conditions and increased sick call attendance. Of the patients seen, 39 per cent had a psychiatric disorder accounting for their attendance to sick call. A total of 43 per cent had anxiety of a chronic and pathologic type. Most individuals in this latter group presented themselves with minor organic illness. It is concluded that emotional disturbances are not only associated with, but in a large part motivate increased attendance at sick call.

## ACKNOWLEDGMENT

ACKNOWLEDGMENT Th h g fl Cl Emm t C L t  
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# MALARIA AMONG TROOPS IN THE FIELD

## Clinical Experiences in the Far East

CONSTANTINE J SAMIOS *Lieutenant MC USNR*

**M**ALARIA was prevalent on Okinawa after World War II. Subsequently, however, preventive medicine units succeeded in almost eradicating the reservoir of the disease, and in the two years preceding this study only one case was reported to have originated among the military on Okinawa.<sup>1</sup> An anopheline mosquito population was present but malaria free during this time.<sup>2</sup> There are many nearby areas in which endemic malaria is well recognized, however, and a constant flow of civilian and military traffic occurs between these and Okinawa. These include (1) the neighboring islands of Yaeyama and Ishigaki of the Ryukyu group, which maintain considerable commercial traffic with Okinawa; (2) Formosa and South Korea, with which a constant interchange of military personnel takes place, and (3) the Philippine Island of Luzon, which has been used as a maneuver area by the Third Marine Division for the past few years.

Since the fall of 1957 the Third Marine Division has held two training maneuvers on the island of Luzon. Operation Phiblink, involving a reinforced regiment of about 5,400 men who took part in ground maneuvers from about 29 November 1957 to 8 December 1957 and Operation Strongback involving the entire Third Marine Division with about 10,000 men participating from about 27 February to 8 March 1958. In addition to these, a base camp of about 500 men consisting of an engineer company and attached units, was maintained from 27 October 1957 to about 17 April 1958. The maneuver took place in central Luzon in the area of Dingalan, the Coronel River Valley, and Laur Cantonment Area, all of which are considered to be endemic for both *Plasmodium vivax* and *Plasmodium falciparum*. In the civilian population, the incidence of vivax and falciparum malaria are approximately equal. The primary vector is the mosquito *Anopheles (myzomela) minimus flavirostris*.

While in the Philippines, all the participating military personnel were required to take the following antimalarial prophylaxis:

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<sup>1</sup> From Department of the Surgeon General and Service Bulletin #1541, 1957, 1542, 1543, 1544, 1545, 1546, 1547, 1548, 1549, 1550, 1551, 1552, 1553, 1554, 1555, 1556, 1557, 1558, 1559, 1560, 1561, 1562, 1563, 1564, 1565, 1566, 1567, 1568, 1569, 1570, 1571, 1572, 1573, 1574, 1575, 1576, 1577, 1578, 1579, 1580, 1581, 1582, 1583, 1584, 1585, 1586, 1587, 1588, 1589, 1590, 1591, 1592, 1593, 1594, 1595, 1596, 1597, 1598, 1599, 1600, 1601, 1602, 1603, 1604, 1605, 1606, 1607, 1608, 1609, 1610, 1611, 1612, 1613, 1614, 1615, 1616, 1617, 1618, 1619, 1620, 1621, 1622, 1623, 1624, 1625, 1626, 1627, 1628, 1629, 1630, 1631, 1632, 1633, 1634, 1635, 1636, 1637, 1638, 1639, 1640, 1641, 1642, 1643, 1644, 1645, 1646, 1647, 1648, 1649, 1650, 1651, 1652, 1653, 1654, 1655, 1656, 1657, 1658, 1659, 1660, 1661, 1662, 1663, 1664, 1665, 1666, 1667, 1668, 1669, 1670, 1671, 1672, 1673, 1674, 1675, 1676, 1677, 1678, 1679, 1680, 1681, 1682, 1683, 1684, 1685, 1686, 1687, 1688, 1689, 1690, 1691, 1692, 1693, 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1 Chloroquine phosphate 0.5 gram weekly as malarial suppressive starting one to two weeks prior to arrival on Luzon and continuing for two weeks after departure. This was given by roster usually on Sunday.

2 Mosquito nets. Base camp personnel were to use a full mosquito net nightly. For tactical reasons most of the infantry units were unable to carry full sized nets but were supposed to use head nets after dark with buttoned long sleeved shirts and bloused trousers. In all about 40 per cent of the men used full nets each night.

3 Mosquito repellent to be applied every three to four hours after dark.

4 Insect spray to be used inside tents and closed spaces.

In general co-operation with these recommended precautions was as good as the tactical situation permitted. A temporary break in malaria control occurred following Typhoon Kit in November 1957 during which almost all the personal equipment of the men in base camp was lost. A one week lapse in chloroquine suppression for most of the men followed and most were without full mosquito nets for about one month afterward. Another break in control occurred when men stayed overnight in a native village.

The following study was made in Okinawa and consists of the presentation of clinical data on 47 consecutive cases of malaria occurring between 1 March 1958 and 15 May 1958. The only case on Okinawa in 1958 before 1 March was a recurrence of chronic malaria contracted elsewhere. After 15 May in spite of 69 consecutive negative peripheral blood smears from men selected at random the entire Third Marine Division was treated with a therapeutic course of chloroquine and primaquine phosphate to preclude the possibility of latent infections. This consisted of one dose of chloroquine 1 gram and daily doses of primaquine 265 mg (15 mg of base) for 14 days by roster. In the past few years most cases of malaria treated on Okinawa occurred during the period covered by this study.

Due to the field conditions under which this study was made some difficulties were encountered. A control group in which chloroquine suppression was not used was impractical. No attempt could be made for long term follow up for recurrent parasitemia or clinical recurrences. Blood levels of chloroquine could not be determined. Most of the data was obtained by clinical interviews of the patients with the inherent but unavoidable risk of inaccuracies in the patients' memory. This was reduced to a minimum by immediate interviews and by an explanation of the study to the patient to achieve the best possible co-operation.

#### CLINICAL MATERIAL

During the period of 1 March to 15 May 1958 45 patients with vivax malaria and 2 with falciparum malaria were treated at Ryukyus Army Hospital. In 45 of these the identification of the plasmodia was made by the laboratory of the hospital. Thirty

nine of the 47 patients were personally interviewed and examined by the author

In all cases, the disease was clinically mild and early. Six patients had not been in an endemically malarial region other than Okinawa for at least one year and had no past history of malaria. One patient had a history of what apparently was malaria, contracted in Korea. Forty, the remainder, had been in Luzon, Philippine Islands, for a period of time varying from 6 to 157 days, averaging 64 days. In one case the first malaria attack occurred only 14 days after arrival on Luzon; in another case it occurred as late as 191 days after arrival in Luzon and 113 days after departure from the area. No significant mean incubation period could be arrived at.

Typically, the patient had a history of malaise and bifrontal headache, worse with exertion and relieved temporarily or not at all by acetylsalicylic acid. This was followed by the development of chilliness and fever. Frequently, gastrointestinal symptoms were present, ranging from nausea or anorexia to abdominal pain and cramps, and loose stools or frank diarrhea (table 1). The chills were seldom "shaking" in character and myalgia was common. In only a very few cases was a definite time pattern of chills and fever established, inasmuch as medical attention was sought quite promptly, usually with the first attack.

TABLE 1. *Clinical findings in 45 cases of vivax malaria*

Symptom or sign	Number of cases	Per cent
Subjective fever	41	91
Malaria and myalgia	40	89
Subjective chilliness	37	82
Headache	32	71
Gastrointestinal symptom	23	51
Splenomegaly	13	29
Elevated serum bilirubin (1 mg per 100 ml or over)	11	24
Concurrent illnesses at onset	17	38

In 17 of the patients (38 per cent) the onset of clinical malaria was preceded for about 48 hours by another illness (table 2) which apparently occurred during the quiescent, latent phase and triggered the acute attack. In only 13 patients (29 per cent) was the spleen palpable.

Upon establishment of the diagnosis of malaria, treatment was started immediately. For vivax malaria, this consisted of chloroquine 1.0 gram immediately, 0.5 gram in 8 hours, and 0.5 gram daily for three doses. Concurrently, primaquine, 15 mg of base was given each morning for 14 days. Most patients continued to be febrile for 12 to 48 hours after start of the treatment, some of them exhibiting the most severe form of the fever during hospital stay at that time. All recovered promptly, the patients felt remarkably well in a very few days. Since the onset of the

ization had no relation to the clinical severity of the illness. In most cases the final doses of primaquine were taken while the patient was back on active duty.

TABLE 2 *I d f r t l l 17 t / 45 p t i s*  
*w th m l*

Con ur t l l	Numb f	P l l c t f ax m lar
Inf t m l	5	11
Ep d m d r r h	4	9
R p tory t f e t	4	9
U t	2	4
G t ur ry t t f	2	4
I o l t c t	1	2
O p t h d ut ryz w th d r r h		f malar

### CHLOROQUINE SUPPRESSION

Chloroquine phosphate has been accepted as the malarial suppressive of choice for troops operating in endemic areas. It is administered orally as a single 0.5 gram enteric coated or plain tablet weekly, achieving peak blood levels of 150 to 250 micrograms per liter. It is stored in the lungs, liver, kidney, and spleen and excreted quite slowly so that after one week the blood level is still 20 to 40 micrograms per liter. For treatment of acute attacks, a level of 5 to 8 micrograms per liter is reportedly adequate. According to standard texts, after an initial two doses chloroquine administered once weekly is supposed to protect against the development of overt malaria from several weeks to many months after the last dose. In our series, however, 50 per cent of the patients developed their first symptoms of malaria less than 24 days after taking their last chloroquine (fig. 1), a period of time during which they should have had ample blood levels to continue to suppress the malaria. Eight patients developed their first symptoms while taking the drug less than one week after their last dose.

Chloroquine in the dosage given does not completely suppress this form of vivax malaria. This may have been due to inadequate absorption from the gastrointestinal tract. It also is evident that chloroquine does significantly decrease the incidence of malaria, as shown by the low over all incidence of only 47 cases in a population of 10,000 men engaged in training simulating combat in an infested malarial region. It also is shown by the extremely low incidence of falciparum malaria—only two cases, one of which was in a patient who had taken his chloroquine only erratically. According to medical intelligence reports, the incidence of falciparum and vivax malaria is approximately equal in the concerned areas, so apparently a large number of cases of falciparum malaria which is potentially the most deadly, may have been prevented.

## CONCURRENT ILLNESSES

It has been noted that 38 per cent of the patients were admitted with initial symptoms due to disease other than malaria (table 2). The most common condition occurring concurrently was infectious mononucleosis, present in five patients (11 per cent). This inci

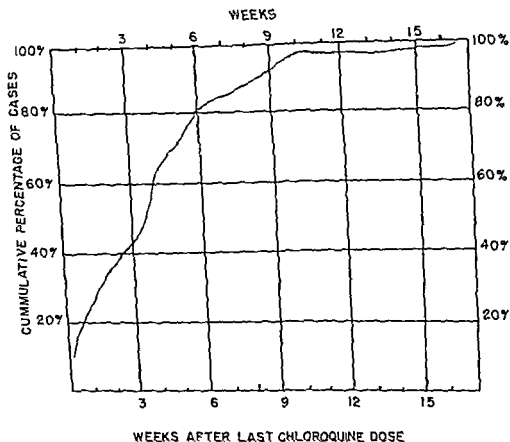


Figure 1 Onset of vax malaria after chloroquine suppression

dence is much higher than would be expected and it may be speculated that the presence of this viral infection in the reticuloendothelial system lowers the resistance and hastens the clinical onset of the *Plasmodium vivax* infection from this system, or vice versa. No significant difference in efficiency of chloroquine suppression could be shown in the cases with concurrent illness.

During the months this study was in progress an island wide epidemic of diarrhea broke out. Four patients with diarrhea subsequently developed overt malaria. No etiologic agent for the diarrhea was incriminated but it is certain that the diarrhea epidemic was not due to gastrointestinal (algid) malaria because of the large number of patients with diarrhea but without malaria. Again, it is believed that the acute illness merely triggered an existing latent plasmodium infection into the full blown clinical illness.

It is noted that two patients had urticaria (giant hives) on admission. No specific allergen was subsequently identified and it may be postulated that the atopic reaction was due to the foreign protein in the plasmodium parasite such as frequently occurs with trichinosis.

### OKINAWA AS AN ENDEMIC AREA

Although only incomplete data are available for the years 1945 to 1955 reports indicate that malaria was prevalent on Okinawa after World War II. By 1952 public health measures had succeeded in nearly eradicating the reservoir so only a few scattered cases among the military population have originated on Okinawa in recent years. No figures are available concerning the incidence if any in the civilian population. However due to the existence of the large number of the potential vector (*Anopheles hyrcanus sinensis*) on the island and the heavy traffic with close by malarial regions the danger of re establishment of the reservoir on Okinawa remains. This year (1958) malaria occurred in six individuals who had not been in other known malarial areas recently. Three of these definitely have had no previous exposure to malaria. Three others have been in malarial areas in the past but on the basis of clinical evidence are thought to have become infected on Okinawa. None of these had symptoms of malaria in the past. It also is possible that one or more of the 38 other cases of vivax malaria attributed to Luzon may have been contracted on Okinawa.

### SUMMARY AND CONCLUSION

In 47 consecutive cases of malaria the use of chloroquine phosphate in the dose schedule of 0.5 gram weekly is evaluated and found to be partly effective in suppressing vivax malaria. However this effect does not seem to be as prolonged as previously indicated. Attacks of clinical malaria were often triggered by incidental infections. The occurrence of six cases of vivax malaria apparently originating on Okinawa is noted as evidence that malaria is once more threatening to become a significant hazard to military personnel there.

#### ACKNOWLEDGMENT

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# ROENTGENOGRAPHIC MANIFESTATIONS OF PULMONARY SARCOIDOSIS

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**S**ARCOIDOSIS is a disease of unknown cause which can affect any organ or system of the body but appears to have a special predilection for the lungs and their lymphatic drainage areas. Pulmonary sarcoidosis usually is a fairly benign process which runs its course with few, if any, symptoms, and undoubtedly is unrecognized in many individuals. Occasionally, however, its manifestations can be troublesome and its outcome serious.

Although the majority of cases of pulmonary sarcoidosis present little problem in diagnosis, there are some in which diagnosis is difficult because of minimal or bizarre roentgenographic appearances. During the past five years, 48 histologically proven cases of sarcoidosis were seen at this hospital. Of these, 40 had thoracic involvement of some type. Roentgenograms of the chest were available for study in 38 cases which form the basis of this report.

## CLINICAL FEATURES

The age, sex, and race distribution of this series is of little significance in the overall evaluation of sarcoidosis because of the high degree of selectivity of our patient population. It has been well established, however, that sarcoidosis is most commonly found in the 20 to 35 year old age group, is more prevalent in females than in males, and in this country shows a much higher percentage incidence in the Negro than in the Caucasian population.

The age range of our patients was from 17 to 39 years, with a mean age of 24 years. Of our patients, 35 were males and three were females. 16 were Negroes.

Of the 38 patients, 11 had symptoms at the time of discovery of their disease. In only five of these, however, were the symptoms significant enough to cause them to seek medical attention. Dyspnea was the chief complaint of one patient; two had a non-productive cough, and two had cough, dyspnea, weakness, and weight loss. The other six patients with symptoms volunteered the information when questioned that they had had an intermittent



dry hacking cough. It was interesting to note that at the time of discovery of disease 27 cases were completely asymptomatic and 33 were discovered on routine chest roentgenograms. This disease often remained asymptomatic throughout its course even though the chest roentgenographic findings were quite marked.

### PATHOLOGIC MATERIAL

The most successful method of histologically identifying this disease in our cases was by scalene node biopsy. Thirty three were proved by scalene node examination, two by liver biopsy, one by skin biopsy, one by lung biopsy, and one by both scalene and liver biopsy.

Microscopically sarcoidosis is characterized by the presence of epithelioid cell tubercles in a tissue or organ. These tubercle like lesions have little if any necrosis and eventually undergo regression by fibrosis. The fibrous tissue formed in the wake of the tubercle rapidly becomes compact and hyalinized with the eventual development of dense scar tissue.

### ROENTGENOGRAPHIC FINDINGS

The roentgenographic appearance of pulmonary sarcoidosis is dependent on the stage of the process and the extent of involvement. The usual course of the disease is characterized by a fairly definite pattern of involvement of thoracic structures. The varying roentgenographic manifestations found initially result from discovery of the disease in one of its several phases.

Enlargement of the hilar and paratracheal lymph nodes with or without minimal lung involvement, is the first thoracic manifestation of sarcoidosis. This adenopathy may be quite striking in appearance. When the disease is seen in its formative stage the nodes may show significant progression in size in a short period of time.

This enlargement of the hilar and paratracheal nodes usually regresses over a period of months or years without roentgenographic evidence of significant lung involvement. Disseminated parenchymal disease subsequently develops in some cases which have node enlargement and will usually appear as the enlarged nodes begin to decrease in size.<sup>3</sup> These parenchymal changes may regress sometimes quite rapidly or they may go into a chronic phase with the eventual formation of pulmonary fibrosis and emphysema.

### MATERIAL

At the time of diagnosis 16 of our patients had only enlarged nodes. In most of these patients both of the hilar and both of the paratracheal areas were involved. However any group or combination of groups of nodes were found to be enlarged. In our cases the left paratracheal chain of nodes was involved as frequently as the right but this was not as evident on the roentgenogram because this area is partially obscured by the aortic arch and pulmonary artery (fig. 1). One of these cases

had such extensive node enlargement with bronchial compression with atelectasis of the right middle lobe and a portion of the right lower lobe (fig. 2).



Figure 1 Sarcoidosis demonstrating bilateral hilar and paratracheal node enlargement. Note the enlarged left paratracheal nodes partially obscured by the aorta and pulmonary artery.

apparently is not common, as there are only two other cases of right middle lobe syndrome due to sarcoidosis reported in the literature.<sup>3</sup>

Five of our cases had enlarged nodes and some minimal lung involvement. This lung involvement consisted of a few scattered patches of parenchymal infiltration and linear fibrostranding, usually confined to the upper lobes (fig. 3).

We observed the development of pulmonary sarcoidosis in five patients, all of whom had normal roentgenograms of the chest within a 4 month period prior to the development of the disease. One of these was a known case of sarcoidosis with liver and ophthalmic involvement. When pulmonary disease developed in this patient, only the left paratracheal node enlarged, remained large for several months, and then regressed. Two patients had node enlargement in all areas.

oped node enlargement and simultaneously some minimal parenchymal infiltration in the upper lobes. One of these latter patients was followed for three years. The nodes disappeared within a year but the parenchymal lesions remained essentially unchanged for two years and then gradually became tiny fibrotic strands.

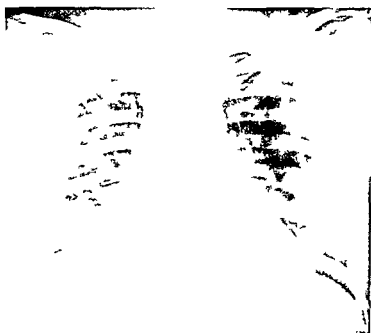


Fig. 2. B. lat. l. h. l. a. d. p. t. h. l. o. d. l. g. e. m. t. a. r.  
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Some form of generalized lung involvement was observed in 17 of our patients. Of these 15 could be classified as having early or acute form of the disease and two as late.

Of the 15 cases of early parenchymal disease eight had definite node enlargement, one changed from predominant node involvement to lung involvement. The nodes receded as the parenchymal disease increased. This change took place within a 9 month period of time.

Three types or patterns of parenchymal disease were observed on the roentgenograms, although some intermixing of the types was present in most cases. A fine reticular pattern predominated in five cases (fig. 4). A coarse reticular pattern usually accompanied by a few small coalescent areas scattered throughout the lungs appeared in six cases (fig. 5). Large patchy areas of increased density with fluffy irregular margins were seen in three cases (figs. 6-8).

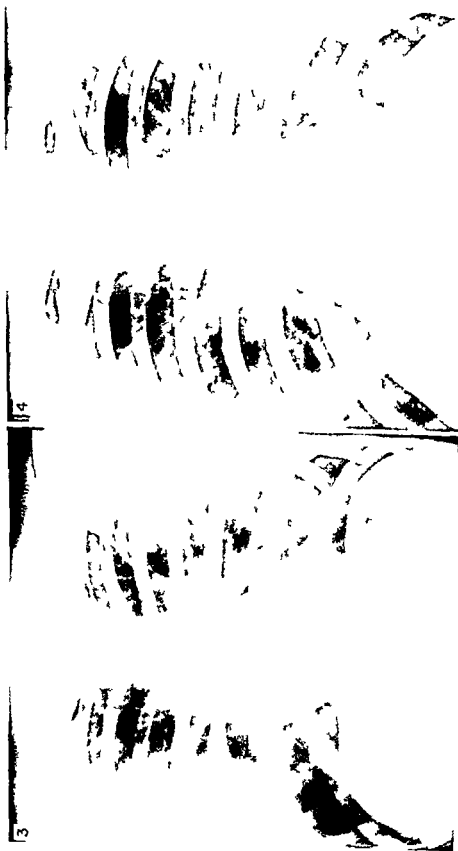
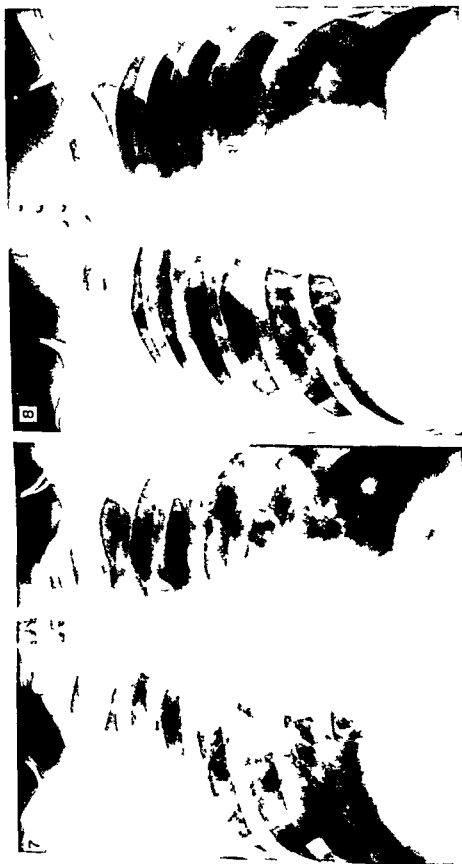


Figure 3 In this case there was simultaneous development of bilateral adenopathy and minimal parenchymal disease of the right upper lobe. Figure 4. Sarcoidosis with diffuse lung involvement manifested as a fine reticular pattern.



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*Figure 7. This case demonstrates sarcoidosis with a nodular type of lung involvement. Hilar and paratracheal node enlargement are present. Figure 8. Same case as figure 7. Two months later the enlargement has been almost completely resolved. The entire disease process. Note the presence of infiltrates on the right. Two patients in this series developed pleural effusion.*

The late stage of this disease is characterized by the occurrence of extensive fibrosis and emphysema (fig 9)

### DIFFERENTIAL DIAGNOSIS

The differential diagnosis of sarcoidosis can be divided into two main groups. Those cases with hilar and paratracheal adenopathy must be differentiated from the adenopathy found in many diseases, but the most important differential is between sarcoidosis and lymphoma. Sarcoidosis uncommonly involves the nodes of the anterior mediastinum whereas the lymphomas often



Fig 9 The chest roentgenogram showing extensive pulmonary fibrosis and emphysema. The paratracheal adenopathy is also visible.

do. Adenopathy in the anterior mediastinum can be identified on the lateral roentgenogram of the chest. Lateral chest roentgenograms were available for study in 36 of our 38 cases. In no instance were the nodes in the anterior mediastinum enlarged although in two cases the paratracheal adenopathy was of such magnitude that it appeared to encroach on the anterior mediastinum.

When parenchymal involvement is present with or without node enlargement sarcoidosis must be differentiated from tuberculosis, coccidioidomycosis, berylliosis, Hamman-Rich idiopathic

pulmonary fibrosis, alveolar cell carcinoma, and pneumonia, depending on the pattern of involvement in each particular case

### SUMMARY

Pulmonary sarcoidosis is a disease which undoubtedly occurs more frequently than is generally recognized. It is frequently asymptomatic and is often discovered on routine roentgenographic examination of the chest.

Pulmonary sarcoidosis appears to follow a fairly definite pattern of involvement of thoracic structures. The initial involvement is manifested on the roentgenogram by enlargement of the hilar and paratracheal nodes with or without some minimal lung involvement. Extensive parenchymal involvement may occur as a later manifestation. This parenchymal involvement is seen in several patterns.

The entire disease process usually regresses over a period of months or years, but occasionally will go into a late or chronic phase characterized by fibrosis and emphysema.

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### DEATHS FROM HARMFUL CHEMICALS

Nearly 8 000 persons in the United States lost their lives from accidental and intentional overexposure to harmful chemicals in 1955. These figures do not include deaths due to food poisoning, acute and chronic alcoholism, or poisoning by venomous animals. Over one half of the listed fatalities were classified as unintentional poisonings; that is, deaths were due to accidents, medical misadventure, and occupational exposures. Since the major portion of all fatal accidental poisonings occur in or around the home, the higher incidence of injury due to medicinal chemicals is greatly influenced by the widespread casualness about the toxic properties of common drugs and easy access to those capable of causing harm.—Bernard E Conley, Morbidity and Mortality From Economic Poisons in the United States. A M A Archives of Industrial Health August 1958.



# THE SUBMAXILLARY GLAND IN NATURALLY ACQUIRED CARNIVORAL RABIES

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**I**NVESTIGATION of rabies has continued since Pasteur's dramatic and classic experiments but advance in fundamental research deriving from fortuitous or acute observations has been meager. Important basic studies have dealt with evidence of the relationship of rabies virus and the parasitized host cell.

Hvden reported that rabies elementary particles are self-reproducing units. They attack the nucleoprotein forming center in the region of the Purkinje cell's nucleolus associated chromatin. Particles rich in desoxyribonucleic acid are formed within the nucleus of the Purkinje cell of a rabbit infected with rabies. Ultraviolet light absorbing spots give a positive Feulgen nuclear stain. Electron microscopy has revealed characteristic vacuoles within Negri inclusions in hippocampal cells of a rabies infected mouse. However study did not substantiate identity of virus elementary bodies. Recent cytochemical investigation of inclusion bodies of rabies confirmed earlier observations that Negri bodies do not give Feulgen positive nuclear reaction and do not contain detectable levels of ribonucleic and desoxyribonucleic acids. The Negri body is neither simple carbohydrate, neutral fat nor crystalline material but is comprised of dry substance, possibly mainly proteins, in larger amount than in surrounding cytoplasm. Negri bodies appear approximately 3 days after demonstration of infective virus in animal tests. The question of the origin of the Negri body is unknown although Negri inclusion bodies almost without exception occur after infection with natural or so called street virus rabies. It is a conspicuous fact that the relation of the Negri body and rabies virus remains obscure. A great amount of work has been directed to the latter question but the central nervous systems of infected animals have not yielded workable clues.

The relationship of the Negri body and virus has proved of extreme complexity to resolve. It may be reasonable to speculate, therefore, that the preferential site of rabies virus development and maturation in the carnivorous host in natural disease has not been sharply identified.

The salivary glands in contrast to brains of rabid animals are noticeable for the comparative neglect that they have received in fundamental research. For example, the Expert Committee on Rabies of the World Health Organization<sup>8</sup> proposes a number of suggestions for future research. The basic research of salivary glands of naturally rabid carnivorous hosts is touched on slightly in connection with ecologic investigation. Neither histopathologic nor immunologic techniques permitting the localization and visual demonstration of the rabies particle or distinctive pathologic biochemical products of infected salivary gland cells have evolved. An important fact is widely known concerning dogs naturally infected with street virus rabies, namely, that the mandibular gland on fresh weight basis frequently contains more infective virus material than brain tissue of the same animal.<sup>9-11</sup> The virus associated with infected submaxillary glands of dogs has high stability and can be stored almost indefinitely at 70°C.<sup>12</sup> Experiments utilizing infected submaxillary gland suspensions as challenge material in rabies immunity research therefore have been conducted.<sup>12-14</sup>

This laboratory has instituted a long term study of rabies virus in the mandibular salivary gland and brain sites of naturally rabid animals. Procedures that effect partial purification and concentration of rabies virus in material from the submaxillary gland have been explored. The characteristic property of the virus from mandibular salivary glands of rabid dogs has been studied. As a consequence of the work reported herein, microscopic corpuscular elements in infected submaxillary glands not previously recognized have been found.<sup>1</sup>

## MATERIAL AND METHODS

**Street Virus Material.** Materials infected with rabies virus were obtained from dogs in Korea with naturally acquired disease. Brain and submaxillary salivary glands were obtained from animals that died from gunfire or following a quarantine period. Wet impression<sup>1</sup> and histopathologic staining procedures were applied to brains of animals for detection of Negri bodies.

**Intracerebral Titration of Virus.** Ten and 20 per cent by weight of each of submaxillary salivary gland and brain were macerated in a Ten Broeck tissue grinder. The sterile diluent comprised 1/150 Sorensen's phosphate buffer pH 7.2-0.85 per cent sodium chloride and 0.63 mg (1,000 units) crystalline potassium penicillin G per ml. Coarse tissue fragments in the homogenate after disintegration in the Ten Broeck grinder, were removed by

centrifugation for 10 minutes at 1 600 r p m in a Model PR 2 International Refrigerated Centrifuge The supernatant was the conventional 10 per cent or 10 tissue suspension Tenfold serial dilutions of tissue homogenate were made in modified Sorensen s buffer solution with penicillin containing in addition bovine serum albumin of about 100 mg per cent nitrogen concentration Inoculums of 0 03 ml of each dilution of tissue suspension were injected intracerebrally in five mice Animals were observed twice daily for 30 days Titters of infectivity, expressed as negative  $\log_{10}$  LD were calculated by the method of Reed and Muench

**Nitrogen Determinations** Suspensions of brain and submaxillary gland tissue of dogs were sampled before and after treatment with Attasorb Nitrogen assay was achieved by a standard macro Kjeldahl procedure Nitrogen was expressed in mg per 100 ml of tissue suspension

**Virus from Submaxillary Gland** The submaxillary salivary gland situated at the posterior border of the dog s mandible is elliptical in shape and grayish yellow or orange in color Histologically it is a mixed type salivary gland comprising physiologic groups of serous and mucus secreting cells The tough fibrous capsule encircling the gland was dissected away The gland tissue was weighed and cut with sharp sterile curved scissors The preliminary mincing rendered the gland tissue suitable for mechanical disintegration of the cell components Five grams of the minced salivary gland were ground up manually with the aid of a 50 ml Ten Broeck grinder Careful manipulation was necessary to avoid accidental breaking of the tissue grinder A modified Sorensen s phosphate buffer solution was used as aqueous diluent It contained Sorensen s M/15 mixture of monobasic potassium phosphate ( $\text{KH}_2\text{PO}_4$ ) 98 ml anhydrous dibasic sodium phosphate ( $\text{NaHPO}_4$ ) 75 ml and distilled water to 1 liter Sodium chloride 8 5 grams was added The final pH was 7 2 Penicillin supplement of 1 000 units per ml minimized bacterial contamination Coarse tissue fragments were removed by low speed centrifugation for 10 minutes at 1 600 r p m The viscid opalescent supernatant was the starting 10 per cent glandular tissue suspension The viscosity noted was derived from the thick and slimy secretion of the mucous glands The homogenate was treated with a chemically inert natural occurring siliceous material described as Attasorb or Attaclay SF Attasorb is a fine powder of particle size of 400 to 600 millimicrons in diameter It possesses high sorptive property for low molecular weight cellular constituents It provided a mechanical trap for cell and nuclear walls and other extraneous tissue fragments A quantity of sterile autoclaved dry Attasorb was added in proportion of 10 grams to 90 ml 10 per cent gland suspension the mixture shaken vigorously by

hand, and centrifuged for 10 minutes at 2 500 r p m — 5 C. The absorbent clay was discarded. The resultant aqueous phase has been termed Attasorb treated supernatant. Attasorb possesses a rare ability to reject high molecular weight, cellular invading, infectious materials such as virus<sup>19</sup> and complex polymerized deoxyribonucleic acid.<sup>20</sup> In the mandibular salivary gland of the rabid dog, Attasorb failed to absorb sub-microscopic granules and distinguishable microscopic elements.<sup>15</sup> The clay absorbed viscous aqueous phase was centrifuged for 1 hour at 17,250 r p m at 5 C, in an International Portable, PP 2 Refrigerated Centrifuge. The centrifugation yielded a clarified but still opalescent viscous aqueous portion designated high-speed supernatant and a small pellet of gelatinous material identified as sedimentable fraction.

## RESULTS

Nitrogen estimations of six preparations each of brain and submaxillary salivary gland are summarized in table 1. The presence or absence of rabies virus in these preparations was established by animal test. Attasorb treatment removed approximately 58 to 71 per cent nitrogen from 20 per cent brain tissue suspensions. The reduction in nitrogen with Attasorb of 10 per cent submaxillary gland suspensions varied from 21 to 78 per cent.

TABLE 1 Nitrogen content of suspensions of brain (A) and submaxillary salivary gland (B) of dogs before and after adsorption with Attasorb

Specimen	Per cent suspension	Total nitrogen <sup>1</sup> (mg/100 ml) Attasorb <sup>2</sup> treatment		Per cent N reduction	Rabies diagnosis by animal test
		Before	After		
1 A	20	115	39	67	Negative
1 B <sup>3</sup>	10	156	81	48	
2 A	20	129	42	68	Negative
2 B	10	138	31	78	
3 A	20	116	41	65	Negative
3 B	10	144	47	68	
4 A	20	122	36	71	Negative
4 B	10	122	84	31	
5 A	20	100	42	58	Positive
5 B	10	82	22	73	
6 A	20	127	4	97	Positive
6 B	10	1	27	97	

<sup>1</sup> Wet weight of specimen before and after treatment with Attasorb.

<sup>2</sup> By micro-Kjeldahl method.

<sup>3</sup> Product of Maxillary gland.

Microscopic corpuscular elements of submaxillary gland of a dog with naturally acquired rabies disease are shown in figure 3

### DISCUSSION

The technic of adsorption with inert siliceous Attasorb has achieved the separation of an apparently nonspecific nitrogen complex salivary gland component without noticeably altering the quality or infectivity and quantity of the rabies-disease in ducing moiety Salivary gland tissue suspensions of dogs are characteristically viscous Variations in reduction in nitrogen

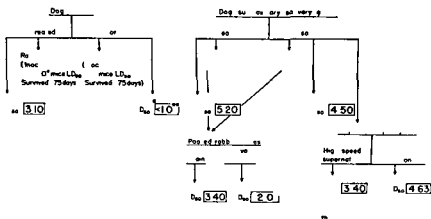


Fig 2 P p ty f i l f t t us 10 p n t i us p ns

content of submaxillary gland component of 31 to 78 per cent may be attributed to a function of the viscosity of the preparations. In contrast separation of nonspecific nitrogenous impurities has yielded infective post Attasorb submaxillary gland suspensions of uniform property to incite rabies disease (table 2). Dog brain suspensions are relatively rich in virus material but are devoid of viscosity. It is not necessarily remarkable that reduction in nitrogen content of brain suspensions is accompanied by loss of detectable levels of the infectious component. This is consistent with the findings of many workers who have attempted to apply purification technics to rabies infected brain tissues. The explanations for the contrasting behavior of rabies infected brain and submaxillary gland suspensions with respect to Attasorb may reside in (1) function of the viscosity of the gland preparations and (2) the possibility that submaxillary gland may in addition to the elementary rabies virus moiety contain a particle of uniform size and weight (fig 3) associated with infectivity not previously recognized.

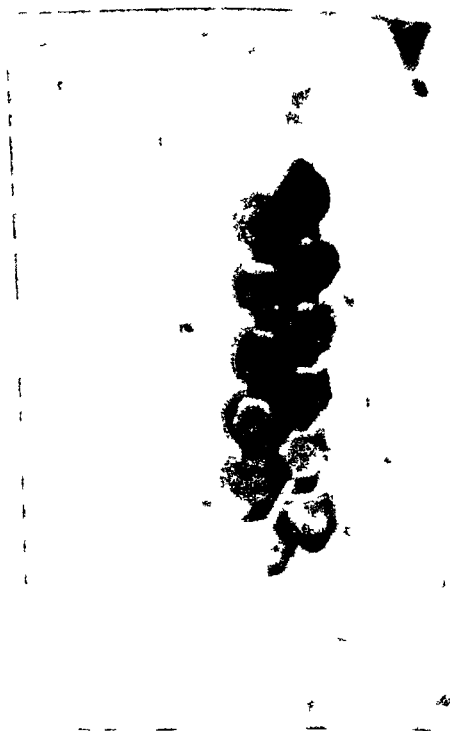


Fig. 3 Agglomerated cellular element from submaxillary salivary gland of a adult dog. Microscopic body section from sedimentation fraction by technique of incubation in 1% anti-arsenic m-phosphate buffer followed by centrifugation for 1 hour at 5000 p.m. at 5°C. Film of wet sediment spread on slide air-dried and fixed with methanol. Staining is achieved by use of a mixture of pyro-B and methyl green basic dyes. Photographed with tungsten light source ( $\times 4860$ )

Investigations of rabid dogs by many workers have disclosed that possibly two important sites are parasitized by the rabies virus entity namely the central nervous system and salivary glands. The background of current fundamental knowledge of rabies virus and the disease which it induces in animals and man lies in basic studies of infected nerve cells. The cells of parasitized salivary glands in rabies are susceptible to disruption by mechanical means. Thus with aid of a simple mechanical device such as a Ten Broeck grinder cell walls and nuclear membranes of parasitized submaxillary gland cells are disintegrated.

Consistent with modern concept of the structure of viruses infected cells accumulate pathologic products in the form of virus proteins possessing property of antigenicity and virus nucleic acids carrying the determinant of infection. Nucleo proteins produced in cells during virus infection have been interpreted to represent the metabolizing and reproducing virus particles. According to Hyden in the central nervous system the Purkinje cell's nucleolus is a principal site of attack of the rabies virus. The nucleolus is in fact a high molecular weight entity enormously enriched in ribonucleic acid. The nucleolus and hypothetical particles of the order of size greater than nucleolus but smaller than nucleus might conceivably be spared disintegration by a tissue grinder. If indeed Attacly SF possesses remarkable sorptive property and capacity to reject nucleic acids it should in submaxillary gland suspension assisted by the natural property of viscosity repel high molecular weight infective nucleotides or previously undescribed virus parasitized nucleotide containing particles of uniform magnitude and weight.

In support of the latter hypothesis it has been demonstrated that a microscopic 2 to 2.5 by 2.5 micron size corpuscular element is present in post-Attasorb submaxillary gland suspensions of rabid dogs. This particle recoverable in the sedimentable fraction of the submaxillary gland is shown to be associated with high infectiousness (table 2 and figs 1 and 2).

The biological events relating to rabies virus maturation and development during incubation in an injured host are not fully understood. Invasion of an infective particle or particles of rabies from an animal bite requires a prolonged and characteristic variable period of tissue migration. The infective moiety must reach a preferential site or sites within the host. Optimal nutritional environment is indispensable if the determinant of infection is to mature and multiply sufficiently to attack the vulnerable central nervous system of the host. What is the exact route or routes of the viral particles tissue migration? Is it in naturally acquired disease restricted to transport along nerve pathways as has been hypothesized? This raises the question of an alternative route of migration of salivary gland particles of elementary or larger size toward an environment particularly

sited for the virus' multiplication and development and survival in nature. The alternative preferential site in natural disease may be hypothesized to be the salivary glands, with the submaxillary gland because of its richness in mucus as well as serous secreting cells, as an optimal site favoring virus self reproduction and survival.

It has been the purpose of this article to point out that the site of the submaxillary salivary gland of naturally rabid dogs and other members of carnivorous reservoir hosts possesses potential for comprehensive fundamental and practical studies of rabies. Basic studies pertaining to relationship of the corpuscular elements of mandibular salivary glands of rabid dogs and rabies virus are now in progress at this laboratory.

### SUMMARY

Concentration of determinant of infection of submaxillary glands of dogs with naturally acquired rabies disease has been accomplished. A chemically inert, natural occurring, siliceous material, endowed with a sorptive characteristic was used in the separation of nonspecific nitrogen component from mechanically disrupted submaxillary glands. Subsequently, high speed centrifugation of submaxillary gland suspension yielded a pellet of gelatinous substance. The latter material, termed sedimentable fraction when derived from the submaxillary gland infected with rabies virus, retained ability to incite rabies disease experimentally. In addition the fraction contained a corpuscular element reactive in anti-rabies serum not previously associated with naturally acquired rabies in dogs.

The background of present knowledge of the nature and properties of rabies virus has been discussed. Fundamental studies of nerve cells of animals infected with rabies have yielded much of known basic facts. Attention has been focused on the fact that mandibular salivary glands of rabid dogs may contain tenfold to a hundredfold more infective rabies LD<sub>50</sub> for mice than an equivalent unit of fresh weight brain tissue. Yet it is remarkable that corresponding fundamental knowledge of the relation of the submaxillary gland cells and rabies virus has been virtually neglected. This paper raises the question of whether the site of the submaxillary salivary gland of naturally rabid dogs possesses potential for comprehensive fundamental, and practical studies of rabies.



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quently experience feast alternating with famine and eat foods to which they are not accustomed. These factors can contribute to gastrointestinal upsets weakening the natural defense against the overgrowth of harmful bacteria.

Another consideration is that just as different geographic areas have different flora and fauna so each soil breeds different crops of bacteria and viruses. The food and water of every region has its own chemical peculiarities and contains different types of microorganisms. The longer a person lives in a certain locality the more he becomes accustomed to the water of the region and becomes immunized to the specific mixture of the local microbes and viruses that are ever present in the food, water and air of his environment and which even the most modern methods of sanitation cannot eradicate completely. The same minute forms of life which are usually innocuous to the resident are likely to be disease producing in a newcomer entering from another bacterial milieu. These factors were more potent in former times before the advent of modern medicine and the knowledge of better purification and preservation of food and drink.

Diarrhea was so common in wars that it became the accepted belief that this condition was induced by fear of battle. In a number of realistic novels scenes are described in which soldiers when pinned down by enemy fire soiled their pants. Medical experience has shown that in most men it was not the emotion of fear but rather the sickness of dysentery that produced these unfortunate accidents. The deathly paleness of the victims was more often caused by abdominal cramps and the weakening effects of dysentery than by fright. Modern army doctors have noted that under conditions of regular food supply and the absence of contagious dysentery cases of diarrhea are the exception among soldiers during battle. Contrary to the popular notion tension, anxiety and fear will loosen the bowels only in a few men. In the majority these emotional states will tend to tighten them up and cause constipation. The diarrheas of battles and of wars were usually produced not by fright but by bacteria.

During the American Civil War diarrhea and dysentery led all other diseases in the medical records of the United States Army. More than 25 per cent of all sickness reports were listed under this diagnosis. There were 1 739 135 recorded cases of acute and chronic diarrhea and dysentery with 44 558 deaths among 2 780 000 Federal soldiers. As great as the occurrence rate of this disease was in the Federal Army it was almost twice as high among the Confederate troops. According to available medical statistics compiled from comparative periods prior to July 1863 the annual number of cases of diarrhea and dysentery averaged 987 per 1 000 (many had repeated attacks) in the Confederate Army compared with 543 per 1 000 in the Union Army. Such a high percentage of disablement weakened the effectiveness of the Confederate Army much more compared with that of

the Federal Army, since the Confederate Army was only half as numerous

Most of the cases of dysentery occurred during the summer and fall months. There are indications that General Lee's troops suffered severely from dysenteric disorders in the early summer of 1863 during the Gettysburg campaign. The Confederate soldiers had been weakened by a bleak winter and a hungry spring spent in war ravaged northern Virginia. In April of that year, only 2 weeks before the battle of Chancellorsville, Lee complained to James A. Seddon, Secretary of War for the Confederacy, that the ration of his soldiers "consists of  $\frac{1}{4}$  lb of bacon, 18 oz of flour, 10 lbs of rice, to each 100 men about every third day, with some few peas and a small amount of dried fruit occasionally as they can be obtained. This may give existence to the troops while idle but will certainly cause them to break down when called upon for exertion."

Such a diet was extremely short on calories and protein. Moreover, it was highly deficient in vitamins. Almost completely lacking was vitamin C contained in fresh fruits and vegetables. This deficiency led to sporadic occurrences of scurvy among the army of northern Virginia, characterized in its classical form by spongy, bleeding gums, and internal hemorrhages. The more common, milder manifestations of vitamin C deficiency were mostly overlooked since they come on gradually and consist of vague symptoms such as fatigue, weakness, pain in the limbs, mental depression, and decreased resistance against infection.

Before the discovery of the vitamins a great part of the population of the temperate zone was suffering periodically from a certain degree of vitamin C deficiency. In the early spring of each year there was a critical period when the fruits and vegetables stored from the previous season were largely used up and the earliest edible green plants had not yet appeared. It has been assumed that the vague and euphemistic term, "spring fever" originated from the observation of this indisposition recurring each spring, a condition which in reality was caused by vitamin C deficiency.

At the time of the Civil War it was known empirically that fresh vegetables and fruits would cure the symptoms of scurvy. Therefore, at the first signs of spring, Confederate soldiers were sent out into the woods to collect sassafras buds, onions, and other wild vegetation.

The costly Confederate victory of Chancellorsville, 2 months before Gettysburg, was barren of strategic results and did not materially change the dismal picture of poor food supply of the army of Lee. According to Douglas S. Freeman, "of all the arguments that weighed with him" (Lee) in favor of the plan to invade Pennsylvania, "the most decisive single one was that he could

no longer feed his army on the Rappahannock. He had to invade the North for provisions regardless of all else. He had to seek food for his undernourished soldiers and fodder for his lean horses in the rich valleys of Pennsylvania untouched by the war.

Their resistance lowered by months of malnutrition and lack of vitamins the hungry soldiers of the South poured into the well stocked villages of Pennsylvania and gorged themselves with food and drink. They spoiled their stomachs unaccustomed to such rich fare and made their weakened gastrointestinal tracts readily susceptible to infection from the ever present germs that cause dysentery.

An eyewitness account exists of a young officer named John Dooley who commanded the rear guard of Pickett's division on its approach to Gettysburg. He complains of his odious and difficult task of rounding up the numerous stragglers and sending them back to their companies. For frequently it happens he wrote that many soldiers leave their ranks through necessity and weakened by diarrhea can scarcely with all their efforts regain their ranks.

Freeman reports that fully 5 000 sulkers and sick contrived to march with the ambulance train from the battlefield of Gettysburg. This number would have represented approximately 10 per cent of Lee's army which was left to retreat. It is likely that a great number of these sulkers and sick were suffering from dysentery. A still greater percentage of the army probably suffered from milder forms of this highly contagious ailment not sick enough to be excused from active duty during the emergency of a critical campaign but weakened and discouraged by abdominal cramps and diarrhea and their efficiency as officers and soldiers greatly impaired.

If the invasion of Pennsylvania was motivated by lack of food the desperate need of shoes for the Confederate soldiers often marching on gaping soles or on bare bleeding feet brought on the Battle of Gettysburg. Napoleon asserted that it needed as slight a provocation as a dog fight to touch off a battle between two hostile armies poised for action. It is well known that the search for shoes caused a Confederate division to collide with Federal cavalry at Gettysburg—and the battle for the shoes was on—expanding into the decisive Battle of Gettysburg a battle which had not been planned on this location by either command.

History books discuss the question of the high strategy of the generals and their mistakes and praise the heroism of the soldiers on both sides. They fail to mention the unromantic factor of comparative medical statistics which gave the North the edge. The army of Meade had a far superior medical service a better system of sanitation and was in much better physical condition than Lee's army. Meade fought on interior lines assuring a regular food supply consisting of meat bread and dehydrated vegetables.

During July 1863 the army of the Potomac was less affected by dysentery than the army of northern Virginia

Except for its one defeat at Antietam, Lee's army had won all previous major battles in spite of inferior numbers. It had made up for this deficiency by its superior mobility, greater offensive spirit and superior leadership. It was a different story at Gettysburg when for once the Confederate Army started the battle with the added advantage of numerical superiority which it maintained until the late afternoon of the second day.

On the afternoon of the first day two Confederate corps attacked and overpowered an outnumbered contingent of Federal troops defending the town of Gettysburg and took the town. A. P. Hill, commander of the victorious third corps who participated in this victory was described as sick and very pale on this day. This could explain his apathy and failure to reorganize his troops for immediate pursuit of the Federal columns that were fleeing in disorder toward the key position of Cemetery Hill.

On the second day of the battle it took two divisions of Longstreet's corps, only a few miles distant, the greater part of the day to get in position for attack, giving Meade time to bring up his reserves, reinforce and extend his line. In spite of this delay Wright's brigade succeeded late in the afternoon, following a desperate struggle to break through the Federal main position east of the Emmitsburg Road. The battle would have been won if the attack had been supported by the adjoining brigades and coordinated with simultaneous attacks of the other corps. There was no such coordination of effort on this occasion, nor all during the Battle of Gettysburg. Posey's brigade next to the successful breakthrough gave only halfhearted support. Mahone's brigade in close proximity stood idly by. Meade was able to bring up his reserves, force back the victorious troops and close the dangerous gap. In the twilight of the same day Early took important Federal positions on Cemetery Hill but was compelled to evacuate them for lack of support from Podes's division at his right.

It is an unanswered question how much the weakening and demoralizing effect of dysentery might have contributed to the strange apathy displayed by officers and soldiers of the Confederate Army at such crucial points of the battle and to the unaccountable hesitancy and lack of resolution of some of the commanders which caused fatal delays and allowed the chance for victory to slip away.

It appeared to some observers, and later critics, that Lee himself did not show during the Battle of Gettysburg his usual energy, generalship and good judgment which he exhibited in previous and in later battles. An eyewitness account of W. W. Blackford, officer on the staff of Jeb Stuart, claims that the commanding general was seriously handicapped in his conduct

of the battle by an attack of severe diarrhea. In his memoirs *War Years with Jeb Stuart* Colonel W. W. Blackford described his experience as follows:

In the supreme hour of battle the Commander in Chief is the soul of an army that is if he is worthy of the army he commands. This being so anything which affects his physical condition at that time must have a powerful influence upon events. We all know the desperately weakening power of severe diarrhea and this General Lee had as I know. When Stuart arrived upon the left flank of the morning of the 2d (July) there followed several cavalry combats and during the evening I was sent to General Lee to report what had happened. I found General Lee at his headquarters near the town but he was in his tent and I was told by one of his staff that I could not see him so I gave my report to this officer either Verble or Taylor. I think it was who took it in to General Lee and then I sat half an hour with them telling of our expedition. When coming on errands of this kind before I had usually given my report to General Lee in person but on this occasion I supposed he was too busy to see me. I was little surprised to see him come out of his tent hurriedly and go to the rear several times while I was there. He walked so much as if he was weak and in pain that I asked one of the gentlemen present what was the matter with him. He told me General Lee was suffering a good deal from attack of diarrhea. This was the evening of the 2nd day of fight and the day before the final contest. Now who in such a condition would not be affected in vigor of both mind and body and will on this account for several things which were behind them or not pushed forward as they should have been the 3rd of July?

Douglas S. Freeman in his introduction to Blackford's memoirs which he calls an *honest narrative* attempts to refute the contention that General Lee was sick during the Battle of Gettysburg and states that no officer of Lee's own staff ever reported any illness of the General during the Gettysburg campaign. He challenges the trustworthiness of Blackford's account of such a fateful incident. From the viewpoint of a medical historian it is hard to understand how an intelligent man like Colonel Blackford, a responsible officer on the staff of Jeb Stuart, could have invented the vivid details surrounding Lee's sickness which Blackford claims to have witnessed under the striking circumstances of a great battle, circumstances that would have made unforgettable the images which the memory received.

The possible explanation of this contradiction could be that diarrhea was so common in the Confederate Army at Gettysburg that it was not thought worth mentioning unless the victim was put completely out of action. The close associates of General Lee may have tended to ignore the embarrassing predicament of their idolized chief, more so as they unconsciously resented so unheroic a situation and they tried to forget it.



## Clinicopathologic Conference

U S Air Force Hospital Wright Patterson Air Force Base, Ohio\*

### COUGH FEVER AND CHEST PAIN

**Summary of Clinical History** A 46 year old widow was admitted to this hospital on 6 March 1956 because of a cough productive of yellow sputum fever, and chest pain of one month's duration. She died in this hospital 13 days after admission, on 19 March. The history obtained on admission revealed that the patient had been seen by her private physician approximately 3 weeks previously, and a roentgenogram of her chest on 20 February had been reported as normal. She had received one injection of penicillin approximately 2 weeks before admission and developed urticaria. One week prior to admission she had experienced chills, right sided pleuritic pain, and increased cough. There was no history of hemoptysis or of recent weight loss.

There was a history of "allergy" of unstated type to penicillin and sulfonamides. She was a moderate smoker (20 cigarettes daily) and used alcohol occasionally. One episode of bronchopneumonia had occurred in 1950. She had toxemia of pregnancy 9 years prior to admission, and labor had been induced for that reason. Following this delivery the patient was said to have experienced "occasional renal difficulty" of an undescribed character.

**Physical Examination** On admission the patient's pulse rate was 88 per minute, temperature, 103 F, and her blood pressure was 120/60 mm Hg. She was well developed and well nourished. She appeared to be acutely ill. No cyanosis or respiratory distress was noted. There was decreased excursion and diminution of breath sounds over the right side of the chest. No rales or pleural

\*At the time of this Conference, Edward L. Olson, USAF (MC), was Commanding Officer of the Laboratory Service Branch Hospital Service Division, Wright Patterson Air Force Base, Ohio.



rubs were heard. The heart was normal in size and there were no murmurs. No abnormalities were noted on abdominal examination. Mild varicosities of the legs were present.

**Laboratory Studies.** Initial laboratory work showed the hemoglobin to be 14.0 grams per 100 ml, sedimentation rate 30 mm per hour, white blood cell count 5,250 per  $\mu$ l with 68 per cent neutrophils and 31 per cent lymphocytes. Urinalysis showed a specific gravity of 1.020, 2+ proteinuria, and no sugar. Microscopic examination of the urine showed occasional red and white blood cells. The blood urea nitrogen was 13 mg per 100 ml. A roentgenogram of the chest showed bilateral clouding of the lower lung fields and evidence of fluid in the right side of chest. Repeat blood studies on 9 March showed the white cell count to be 21,750 per  $\mu$ l with 95 per cent neutrophils, 23 per cent of which were band forms.

**Course in Hospital.** The patient was placed on tetracycline initially at an oral dosage of 0.5 gram every six hours. On 7 March bronchoscopy was attempted, but a great deal of purulent exudate was encountered in the entire tracheobronchial tree and severe coughing developed. The air passages could not be visualized satisfactorily. A thoracotomy was performed on 7 March under local anesthesia to establish drainage of the right pleural space. At operation the right lower lobe appeared atelectatic. Culture of a small amount of fluid removed from the right pleural space yielded a growth of hemolytic *Staphylococcus aureus* (*Micrococcus pyogenes* var. *aureus*). The abundance of these organisms in the culture was not stated. The patient did poorly and the bilateral pulmonary infiltration extended, as shown by repeated roentgenographic examination of the chest. On 8 March therapy was altered to include erythromycin and Chloromycetin (brand of chloramphenicol) by mouth and bacitracin via nebulizer. Respiratory distress and laryngeal obstruction developed. A tracheotomy was performed on 10 March and antibiotic therapy was altered to consist of 0.75 gram of streptomycin, 1 gram of Chloromycetin, and 200 mg of erythromycin each every six hours intramuscularly and 10,000 units of bacitracin via nebulizer every six hours.

On 14 March the urine output diminished to 300 ml and gross hematuria was noted. The maximum urine output from this time until death did not exceed 500 ml in any 24 hour period. On 14 March 500 ml of whole blood was administered and streptomycin and bacitracin were stopped at that time. On 16 March many rales were audible in the chest and 2+ pitting edema of the ankles was noted. The patient was then digitalized. On 17 March Chloromycetin therapy was stopped.

The patient continued to deteriorate slowly and an episode of cessation of pulse with no recordable blood pressure occurred at 1615 hours on 18 March. After this episode the blood pressure fluctuated between 50/0 and 160/40 mm Hg despite the intravenous use of norepinephrine and the patient died at 1655 hours on 19 March.

Laboratory studies on the day of death revealed a hemoglobin of 10.2 grams per 100 ml, and a white blood cell count of 19,300 per  $\mu$ l, with 57 per cent band forms. Blood chemistry studies revealed the following values: sodium, 125 mEq per liter; chloride, 106 mEq per liter; blood urea nitrogen, 97.5 mg per 100 ml; calcium, 9.0 mg per 100 ml; and phosphorus, 11.4 mg per 100 ml. Carbon dioxide content was 38 volumes per cent. Urinalysis showed a specific gravity of 1.010 and 4 plus proteinuria, and innumerable red blood cells were noted in the microscopic examination.

#### DISCUSSION

Docto Shirley: To review the salient facts of the protocol we have a 46-year-old woman who died after a 6 week illness. One month prior to admission, fever, chest pain and a cough productive of yellow sputum began. She received one injection of penicillin about two weeks after the onset of her illness, which caused urticaria, so she received no more penicillin. Three weeks prior to admission, after one week of illness, the roentgenogram of her chest was interpreted as normal. A week before admission there was increased cough, chills and pleuritic pain in the right side of the chest.

The initial laboratory work showed a markedly elevated sedimentation rate of 50. The white blood cell count, 5,250, which was normal, showed 60 per cent neutrophils and 31 per cent lymphocytes, indicating an infectious process with little total white cell response. There was no eosinophilia. The specific gravity of the urine was 1.020, which combined with 2 plus proteinuria shows that the kidneys were not functioning too well. Three days later she had 21,000 white blood cells per  $\mu$ l, with 75 per cent neutrophils. 23 per cent of these neutrophils were band forms. The blood urea nitrogen was normal. Admission chest roentgenogram showed clouding of the lower lung fields and some fluid in the right side of the chest. The day after admission bronchoscopy was attempted but not completed because of a large volume of pus in the tracheobronchial tree and the inducing of a severe cough in the patient. A thoracotomy was performed to drain the right pleural space. Only a small amount of fluid was collected. At that time the right lower lobe was atelectatic. Hemolytic *Staphylococcus aureus* was grown from the fluid obtained. The patient was treated with various antibiotics and benefited little from them. On 14 March, 8 days after admission, she began to go into renal failure. The urine output dropped to 300 ml and hematuria was noted. From then until she died, her urine output was not over 500 ml per day. On 16 March rales throughout the chest and 2 plus edema of the ankles were noted. The patient was digitalized. Two days later the pulse and blood pressure dropped suddenly and support with norepinephrine became necessary. In spite of this therapy she died the following day.

Final laboratory studies indicated the carbon dioxide was decreased to 38 volume per cent, the blood phosphorus was elevated, and a uri-

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Docto Fl agon Would you care to make an exact diagnosis for the cause of renal failure? It is your impression that it was due to multiple renal abscesses?

Doctor Shirley Yes

D cto Flanagan Dr Randolph, would you like to show the roent genograms?

Doctor Ra d lph Serial films dating from the day of admission to the day of death are available on this patient. The admission film reveals consolidation of the right lower lobe possibly also with some involvement of the right middle lobe. There is infiltration in the left lower lobe. Mediastinal structures are normal and the trachea is in the midline. This patient has an azygos lobe. A small amount of pleural fluid also is present on the right side. A thoracotomy was performed on the day following admission. This film shows a new finding on the left—an infiltration in the left mid lung field and by its distribution suggests it is in the superior division of the left lower lobe which in turn suggests aspiration pneumonia. A second film made on the same day shows the upper portion of the abdomen. Although it doesn't completely exclude the diagnosis of subdiaphragmatic or liver abscess which has ruptured up through the diaphragm it does not support it. On 9 March we see a finding which was not present before. In the upper portion of this consolidated right lower lobe there is an ovoid translucency which could well be a small abscess or because the patient has had a thoracotomy could possibly represent a loculated air bubble. On a film three days later after the patient has had a tracheotomy there has been increase in size of this translucency. Other changes have occurred a clearing of the left mid lung infiltration the azygos vein has increased in size from that seen on the first film and there are small patchy infiltrations in the right upper lobe which suggest pulmonary edema. The protocol tells us this patient began to go into cardiac failure and this dilatation of the azygos vein is compatible with it. Later examinations show progression of the pulmonary edema. No clear cut abscess is seen on the later films nor on the film of the day of death.

The roentgenographic findings are compatible with the diagnosis of staphylococcal pneumonia. Other possibilities are massive septic pulmonary embolus an aspiration pneumonia or a subdiaphragmatic abscess extending into the chest.

A Phy lclo : You say that a subdiaphragmatic abscess is still a possibility? Did you not say the film of the abdomen ruled it out?

D cto Ra d olph I saw nothing on the film of the abdomen to suggest a subdiaphragmatic abscess let's put it that way.

D cto Scholet This patient presents a few very interesting problems. The most important is the question of primary cause of the disease.

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C pt J h F Fl g USAF (MC) Pathol g i t  
Capt Charles L. R d lph Jr USAF (MC) R d ol g st  
Capt A lbert Schal t USAF (MC) M d c l S r

Then the cause and mechanism of her renal involvement the relationship of the renal involvement to her previous history of toxemia of pregnancy and the treatment should be considered in the hospital. This patient was a 46-year-old woman who apparently had no major illness prior to her admission to the hospital with an acute illness. Her illness lasted only 12 days. What diseases could cause such a rapid demise? The first and most important suspicion is a Dr. Shirley mentioned. There are two types of pneumonia that would present problems both in diagnosis and therapy. One notorious example is the phylococcal pneumonia. This pneumonia is seen in debilitated persons as a secondary pneumonia in patients with malignant diseases. I should mention that perhaps the explanation for the first normal white blood cell count that Dr. Shirley referred to followed by an increased leukocytosis during the patient's course of illness could be found in secondary staphylococcal pneumonia after influenza A virus disease followed by a secondary infection would cause such a leukocytotic response.

Another type of severe pneumonia is due to Friedländer's bacillus (*Klebsiella pneumoniae*). This occurs more frequently in males than in females, especially in alcoholics. Frequently it is a suppurative pneumonia but the sputum of the patient of the sputum given in the protocol is not like the jellylike, tenacious and purulent appearance of the sputum seen in Friedländer's pneumonia. I don't know whether a sputum smear was made during the patient's stay in the hospital but usually there is not much difficulty in demonstrating Friedländer's bacilli in the patient's sputum. Mycotic pneumonia occurs frequently in people who are debilitated by malignant diseases but usually do not have a course as rapid with high fever but rather a prolonged course. This woman did not have a debilitating disease in the past therefore I would rule out these possibilities. Vascular disease of the lung due to multiple emboli or massive infarction can be mentioned but there are no peripheral signs or any inflammatory diseases of the lower extremities which might be the source of an embolus of the lung nor a history of hemiparesis which usually accompanies lung embolization. In a massive pulmonary infarction the history would be much more dramatic as far as her previous stress is concerned. Another vascular disease—periarteritis—usually has a more prolonged course. It would not cause this type of picture and also would be accompanied by renal changes and by high blood pressure. Wagner's type of glomerulonephritis is accompanied by ulceration of the nose and sinuses which this patient did not have. Malignancy also was mentioned before and here alveolar cell carcinoma should be mentioned. The course usually is not so rapid as was the case in this woman. I don't know whether or not she was going to a physician six weeks before she entered the hospital. Interstitial fibrosis of Hamman and Rich usually has a slow progressive course. Although a case of rapidly fatal Hamman and Rich type of interstitial fibrosis with necrosis has been reported. That patient was much more cyanotic and her fever was a course different from that seen in our patient.

Tuberculous pneumonia even if it is fatal is more slowly progressive and there are only a few records showing leukocytosis. High in this woman had. As to her treatment in the hospital—I wonder whether it is wise to bronchoscope a patient who has such a high

fever and is in respiratory distress unless there is a definite sign that removal of a foreign body is required because it may add more to the already present respiratory distress I believe the same is true for a thoracotomy which is apt to induce a pneumothorax again adding to the respiratory difficulties A great part of such a patient's lung is then out of circulation and the blood cannot be oxygenated Perhaps oxygen treatment under careful management keeping in mind oxygen intoxication in anoxic patients would be the therapy of choice The variety of antibiotics that this woman received emphasizes the fact that we do not have adequate therapy for staphylococcus infections in general especially those occurring in hospitals *Staphylococcus aureus* was cultured from this patient's pleural fluid and it is a notoriously difficult bacteria to eliminate

It is interesting to note that this woman had renal difficulty nine years prior to her admission. What type of renal difficulty did she have? Usually toxemias of pregnancy are not renal illnesses per se, although patients have convulsions and albuminuria. Teel and Reid<sup>3</sup> reported 80 such cases in which the patients recovered completely after their delivery. Usually they don't have any more difficulty except when toxemia of pregnancy occurs in a patient with underlying hypertension or pyelonephritis or other renal disease. Therefore, I would not attach any significance to the past history of renal difficulties in this woman if her present illness hadn't terminated in renal failure. I don't think that she had renal disease on admission to the hospital.

Now some comments about her death and treatment in her final days. There are two conditions that might cause the symptoms she presented during her last few days of life. In an overwhelming toxemia one must think of acute renal insufficiency, a type of acute tubular necrosis. Another condition that might have caused her renal symptoms is a low sodium syndrome causing a state of shock and a fall of renal output. Another possibility is bilateral adrenal insufficiency with hemorrhage, inasmuch as the laboratory data show she did have a low sodium level with hypotension. In summary, my final diagnosis would be staphylococcal pneumonia with bilateral adrenal hemorrhage. I don't know the cause of her heart failure, perhaps overhydration with low urinary output, general respiratory distress, and infection could produce heart failure in a woman who did not have previous heart disease.

Doct Fla go Dr Tobin would you like to make a comment on this case?

D 1 r T bi First I would like to defend doing a bronchoscopy on a patient with staphylococcal pneumonia. These patients sometimes get a thick exudate they just can't cough up. I remember one case in which bronchoscopy extracted sort of a cast of the bronchial tree composed of thickened fibrous mucus and the patient obtained relief even though he was very sick at the time. I thought it well worth doing. No one mentioned bacitracin as a possible contribution to this patient's renal damage. It was used. I'm sure it caused the doctors were

perate to find something to combat the staphylococci. Using it as an inhalant gives rapid absorption and once it is absorbed one is apt to get kidney damage. It was about three days after treatment with bacitracin that the urine output fell. I blame bacitracin for this. I think renal failure was the immediate cause of death. Staphylococcal pneumonias probably have a 75 per cent mortality rate. They can occur in young men who are not debilitated and result in very rapid death. The patients who recover often have permanent fibrotic damage of the lung.

**Dr. Fligson:** Would you like to say something about renal failure or what the basis might be?

**Dr. Tibbitts:** I thought the basis was the toxic effect of bacitracin. The patient previously had some albuminuria which might have been explained on the basis of fever. I think the real difficulty started after she received bacitracin and most of the damage was due to it.

**Dr. McKay:** One thing no one seems to have considered is the possibility that this disease initially was primarily in the kidney and secondarily in the lung. I'll grant that the initial urinalysis was not spectacular but I don't think anyone would question that it was abnormal. Albumin and red and white blood cells were found which could very well go along with a chronic kidney disease, probably a chronic low grade pyelonephritis which then erupted by hematogenous means and resulted in her death. The possibility of the kidney lesion being the initial lesion definitely should be considered.

**Dr. Shirl:** Yes diagnosis.

Staphylococcal pneumonia with metastatic kidney abscesses.

**Dr. Schlitt:** Yes diagnosis.

Staphylococcal pneumonia with adrenal failure and acute renal failure secondary to acute tubular necrosis.

#### PATHOLOGIC FINDINGS

**Dr. Fligson:** At autopsy the body was that of a moderately obese 46-year-old woman. A few ecchymotic areas were present over the umbilical fossa and a slight degree of pitting edema was seen over the tibia bilaterally. External examination also showed the poorly healed right thoracotomy incision which broke open by gentle manipulation. There was a tracheotomy incision in the neck. The lungs showed rather impressive findings. The entire tracheobronchial tree was almost completely filled with purulent debris and mucoid material and the right lower and right middle lobes and the left lower lobe were bulky, firm, noncrepitant and showed multiple areas of abscess formation surrounding the bronchi. These areas shelled out readily to reveal cavities which measured up to 2 cm in diameter. At this point I might say that the culture from one of these abscessed areas yielded a few colonies of hemolytic *Staphylococcus aureus*.

and a moderate growth of *Escherichia coli*. The upper lobes of the lungs showed a considerable degree of compensatory emphysema. There was a mild amount of pleural effusion on both sides of the chest with a few adhesions of the pleura to the chest wall.

The adrenals were considerably enlarged and contained several large discrete golden nodules. There was a marked increase in weight of the adrenals to 30 grams (normal weight about 12 grams). The kidneys showed rather unexpected findings. They were enlarged to almost twice the normal weight (left 316 grams right 270 grams). Both were swollen, quite pale, and showed multiple punctate subcapsular hemorrhages. The brain showed the presence of a cyst in the third ventricle which will be described later.

I think first it would be well to discuss the fundamental infectious process in the lungs. Histologically the lungs presented a typical pattern of septic pneumonia with findings that indicate the process was of considerable duration. The right middle, right lower, and left lower lobes showed multiple large areas of abscess (fig. 1) formation.



Fig. 1 Section of lung showing edge of abscess

distributed about the bronchi. In many cases these areas were enclosed in fairly well developed connective tissue capsules. Most of the small and medium-sized bronchi were filled with partially organized purulent material. Areas of pulmonary parenchyma not directly involved by abscess formation showed diffuse bronchopneumonia with extensive organization. No microorganisms could be identified in any of the sections.

This case serves to emphasize that *Staphylococcus aureus* is still an important cause of disease in men despite the widespread use of antibiotics. Rogers collected highly significant data from experience



at the New York Hospital with staphylococcal disease by examining the records for selected years in the pre and post antibiotic periods. During the period immediately before the development of penicillin he found that the mortality rate in adults from staphylococcal bacteremia at the New York Hospital was 69 per cent and in the period from 1949 to 1955 it was 70 per cent. More striking figures were seen in staphylococcal pneumonia in which case the preantibiotic mortality was 30 per cent and the post antibiotic mortality rate was 92.3 per cent. Spink stated that the mortality with staphylococcal septicemia remained (in 1954) at 50 to 90 per cent at the University of Minnesota despite the use of antibiotics. In evaluating the importance of these studies one must consider the very significant fact that the primary staphylococcal bacteremia and pneumonia were frequent in the pre antibiotic period while primary infection became much more rare in the antibiotic period and the more common situation was to find staphylococcal infection as the terminal process in leukemia carcinoma uremia and debilitating diseases of the aged. Despite this weighting of the mortality figure by the presence of serious primary diseases it is evident that staphylococcal infection is still a serious problem in patient management.

One of the primary factors in continued high mortality rates from staphylococcal disease is the emergence of antibiotic resistance strains of the organism. In the early 1940's practically no strains of staphylococci were resistant in vitro to the therapeutic dose of penicillin while several studies in the last few years have shown that at least 50 to 70 per cent of the staphylococci isolated in hospitals are resistant to penicillin. Erythromycin also has become less effective with the emergence of resistant strains. Antibiotic resistance is such a high percentage of the organisms makes it almost mandatory that it is late the organism and determine antibiotic sensitivity before undertaking a long course of therapy.

What properties does the organism possess that make it such a serious invader of the body? Many questions are still unanswered. We know however that the organism in culture capable of elaborating a complex group of toxins and metabolites which possibly assist the organism in setting up infection. Among these products are hemolysins, leukocidins, dermonecrotic toxin, fibrinolysin, hyaluronidase and enterotoxin. All of these substances are more common only found in pathogenic organisms isolated from infections in man than in the nonpathogenic strains but the occurrence of these cellular products is highly variable and they may appear singly or together in a single strain. Within the past few years the occurrence of coagulase in a strain has been accepted as one of the most reliable criteria of pathogenicity. Ninety to 95 per cent of pathogenic strains possess the ability to coagulate citrated rabbit or human plasma in 1 to 3 hours after inoculation of the plasma with an equal volume of broth culture. Tologically one could reach that this ability to coagulate plasma is due to wall effects of the organism on the body and prevent contact between the organisms and the body defense mechanism. This is also considerable evidence that the staphylococcus is able to have several foci in the tissues shortly after infection.

so that the body defense mechanisms and antimicrobial agents act at a considerable disadvantage. Coagulase may play an important role in this sequestration of the organisms but the relationship is not yet clear. Coagulase and the toxic products of the staphylococci have largely been identified by their biologic effects while their chemical structure and relative importance in determining the course of the disease are still unknown. So we see that even the major determinants of staphylococcal infection are poorly understood and what is more important we see that deep staphylococcal infection even with the most enlightened therapy is still accompanied by a high mortality rate.

Histologic examination of the kidneys in our patient revealed an unusual complication of staphylococcal infection. The characteristic lesion in the kidneys consisted of anemia of the glomeruli, marked exudation of neutrophils in the glomeruli, hemorrhage into Bowman's space (fig. 2), marked dispersion and vacuolation of the cytoplasm



Fig. 2. Section of the kidney showing hemorrhage into Bowman's space

in the tubular cells and many red blood cell casts in the tubules (fig. 3). Nearly every nephron showed at least some of these alterations. Careful examination showed no evidence of acute tubular necrosis or of toxic tubular damage. The most common organism associated with the development of glomerulonephritis is *Streptococcus pyogenes* of type 12 or type 4, with at most 1 or 2 per cent of acute glomerulonephritis being ascribed to staphylococcal infection. Nothing in the clinical history or hospital course of this patient indicated recent streptococcal infection and it seems reasonable to assume that the renal disease was an outcome of staphylococcal infection in this case.

Histologically the adrenal glands showed marked thickening of the cortical layer by diffuse hyperplasia and by the presence of multiple unencapsulated nodules composed of cortical cells. We are unable to arrive at any conclusion regarding the level of hormone production by the hyperplastic adrenals inasmuch as no satisfactory histochemical method of tissue adrenal hormone assay is available.

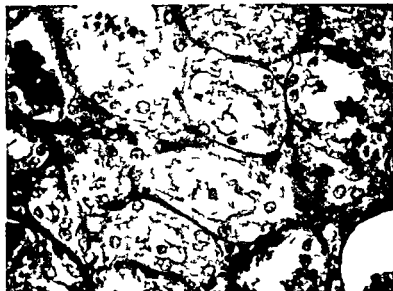


Fig. 3. Section showing marked degeneration and accumulation of the cytoplasmic material in the blood vessel.

Examination of the brain showed a 1.5 cm cyst in the third ventricle which was lined by a thin layer of cuboidal epithelium and was filled with colloid material. Colloid cysts of this character arise from persistent fetal structure; the parapathy is which is more highly developed in the third ventricle of lower animals. These cysts may occasionally function as ball valves obstructing the outflow of cerebrospinal fluid through the aqueduct of Sylvius or the interventricular foramina and producing paroxysmal headache. The headaches may sometime be relieved by changing the position of the head. The cyst in this particular case could never have functioned as a valve because it was firmly attached at several points to the wall of the third ventricle and was not suspended by a single slender stalk as in the usual case.

In summary we have a case of organizing bronchopneumonia complicated by abscess formation involving extensive areas in both lungs. This infection was proved by negative smears and positive culture to be due to hemolytic *Staphylococcus aureus*. The pulmonary infection was complicated by the development of acute diffuse glomerulonephritis. Nodular hyperplasia of the adrenals and colloid cyst of the third ventricle were incidental findings.

## Pathologic Diagnoses

- 1 Bronchopneumonia organizing with abscess formation due to *Staphylococcus aureus* (*Micrococcus pyogenes* var *aureus*)
- 2 Acute diffuse hemorrhagic glomerulonephritis
- 3 Nodular hyperplasia of the adrenals
- 4 Colloid cyst of the third ventricle

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## PLIGHT OF THE CAPTURED AIRMAN

Special survival training including training that prepares a man for the eventuality of becoming a prisoner of war is a by product of modern warfare and is a particular problem of the Air Force. Flying over enemy territory with the constant hazard of forced landing or parachute escape from a damaged aircraft the airman continually faces a potential survival situation. Yet ordinary basic training gives him only rudimentary skills in the use of weapons for self-defense. It does not condition him for long marches and highly uncomfortable bivouacs. The flyer has not had any close contact with the enemy or his terrain; he is not toughened by the rigors of ground warfare. There is a violent contrast between his combat situation in an aircraft and his survival situation on the ground. Furthermore, a future conflict may confront our airmen with the possibility of capture by an enemy who has developed psychological warfare to the greatest extent in history and who continues to wage this warfare unrelentingly against the prisoner who falls into his hands.—Louis Jolyon West, *Psychiatric Aspects of Training for Honorable Survival as a Prisoner of War*, *The American Journal of Psychiatry* October 1958.

## Departments

### GEN TWITCHELL HEADS MILITARY SURGEONS MEETING DEVOTED TO SPACE AGE PROBLEMS

Brigadier General Harold H. Twitchell, USAF (MC), surgeon of the U. S. Air Forces in Europe, was installed as president of the Association of Military Surgeons at the close of the society's 65th annual meeting in Washington last month. He succeeded Colonel Charles R. Meller, MC, USA (Ret.) of the Veterans Administration, who presided at the convention which drew 2,000 delegates to hear papers devoted to the theme of Dynamic Medicine and Rehabilitation in the Space Age.



General Twitchell

Lieutenant Colonel Carl W. Hughes, MC, USA, chief of general surgery at Tripler U. S. Army Hospital, won the Sir Henry Wellcome Medical Gold Prize for his essay on the subject of vascular surgery in the medical services. The Gorgas Medal established by the Wyeth Laboratories for distinguished work in preventive medicine was awarded to Lieutenant Commander John H. Ebersole, MC, USN, medical officer of the U. S. S. *Seawolf*, who organized the medical departments of the first two nuclear powered submarines.

The Major Louis Livingston Seaman Prize was given Colonel R. Lin L. Bauchspies, MC, USA, commanding officer of the U. S. Army Hospital Nubruck, Germany, for his series of articles, "The Courageous Medics of Anzio," that appeared in *Military Medicine*. The 1958 Stitt Award established by the Pfizer Laboratories Division, Charles Pfizer and Company, in honor of the late Rear Admiral Edward Rhodes Stitt, was presented to Captain George L. Calvey, MC, USN, chief of medicine, U. S. Naval Hospital, St. Albans, N. Y., for his clinical research in the antibiotics combining streptococcal pneumonia.

Colonel William H. Lawton, USAF (MC) (Ret.), who died on 6 November, had been chosen as the 1958 winner of the McLester Award.



Col Hughes



Col Ebersole



Col Bachspies

from J B Roetig Company Division Charles Pfizer and Company  
The late Col Lawton was honored for his work in hypoglycemia and  
its effect on the accident rate in the Air Force Training Command  
The Founders Medal was presented to Colonel George B Green  
USAF (MC) for his contributions to military medicine and for  
meritorious service to the Association

The meeting opened with an address by General Alfred M Gruenther  
USA (Ret) president of the American Red Cross who was introduced  
by Major General Howard McC Snyder USA (Ret) physician to the  
President Major General George F Lull MC USA (Ret) assistant  
to the president of the American Medical Association served as  
moderator of the panel of speakers which included the surgeons general  
of the military departments and the Public Health Service and the  
chief medical director of the Veterans Administration "The Changing  
Medicare Program" was the subject of a timely presentation by Brig  
adier General Floyd L Wergeland MC USA director of Medicare  
Major General Wilford F Hall USAF (MC) served as chairman of a  
panel of experts for the discussion of Occupational Health Problems  
in Space Flight and Brigadier General Don Flickinger USAF (MC)  
headed a symposium on Problems of Space



Capt Cal



Col Lawton



Col

## ADM RALPH MALONE RETIRES, SUCCEEDED AS NAVY DENTAL CHIEF BY ADM SCHANTZ

Rear Admiral Ralph W. Malone, Assistant Chief of the Bureau of Medicine and Surgery for Dentistry and Chief of the Dental Division since March 1955, retired on 1 November after 32 years of service. He was succeeded by Rear Admiral Curtiss W. Schantz who has been commanding officer of the U. S. Naval Dental School, National Naval Medical Center, Bethesda, Maryland.



Adm. I M I

During his long service, Admiral Malone provided outstanding leadership and guidance to the Navy Dental Corps. He directed Operation Bulldozer, which raised the strength of the regular corps to more than 1,000 officers and sponsored a training program in mass casualty care. In World War II, while assigned to the USS *New Jersey*, he participated in the campaigns at Kwajalein and Truk Islands. Earlier in his career, one of his three tours of duty was as an instructor in crown and bridge dentistry at the Naval Dental School. He served personally as dentist for President Franklin D. Roosevelt.



Adm. I S hant

Admiral Schantz, in his 28 years of active duty, has had broad experience as a dentist, a leader, and as a dental educator. In World War II, he headed the Dental Department of the Naval Training Center, Great Lakes, Illinois, where he organized and administered the largest group dental practice in existence with over 500 dental officers on duty. During the Korean Conflict, he served as fleet and force dental officer for the Pacific Fleet and supervised the rapid expansion of dental facilities to support the Marines in Korea and the Fleet in the Far East.

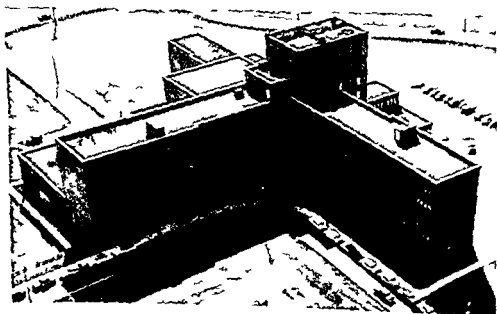
On 31 October, in an impressive change of command ceremony, Admiral Schantz, who was promoted on 1 November, relinquished command of the Naval Dental School to Captain Eric G. F. Pollard, DC USN, his executive officer for the past two years. Guests attending the ceremony included Dr. Frank B. Berry, Assistant Secretary of Defense (Health and Medical); Major General James M. Epply, and James S. Cathroe, Army and Air Force dental chiefs; Dr. Clemens V. Rult, Dean, Georgetown University School of Dentistry; Dr. Bruno Floria, President, District of Columbia Dental Society; and Dr. C. Willard Camlier, American Dental Association.

## KOSSUTH HEADS CIVILIAN MEDICAL GROUP



*Colonel Kossuth*

Colonel Louis C. Kossuth USAF (MC) was installed recently as president of the American College of Preventive Medicine at its annual meeting in St. Louis. The Deputy Command Surgeon of the Air Defense Command is the first military officer on active duty to be chosen for this office. Members of the American College of Preventive Medicine which was formed in 1954 represent the fields of public health, aviation medicine and occupational medicine. Most military members are specialists in aviation medicine as is Dr. Kossuth, a flight surgeon who has served in the Air Force since 1941. Prior to his present assignment, he was deputy commandant of the School of Aviation Medicine. He is a former chief of preventive medicine at USAF and USAFE Headquarters.



**NEW ANDREWS AFB HOSPITAL** Here is the new 250 bed hospital at Andrews Air Force Base, Washington, D. C. which was dedicated in ceremonies on 7 November by Major General Olin F. McNay, deputy surgeon of the Air Force. The five-story air conditioned brick structure which replaces the "old War II hospital" at Andrews Air Force Base contains the most modern integrated medical care. Colonel Audrey J. Jones, USAF (MC) is the hospital commander.



## ARMY NAMES NEW SPECIALIST CORPS CHIEF

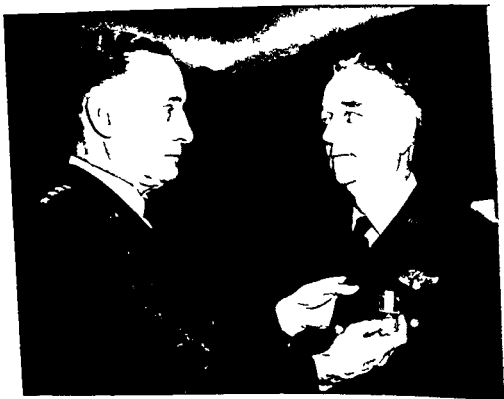
Colonel Ruth A. Robinson has been named the fourth chief of the Army Medical Specialist Corps, succeeding Lieutenant Colonel Herbert S. Lee, now assigned to the Army Medical Service Historical Unit at Walter Reed Army Medical Center. For the past three years, Colonel Robinson has been chief occupational therapist at Walter Reed Army Hospital and had previously served in the same capacity at Fitzsimons Army Hospital and Brooke Army Hospital. Before her appointment in 1948 to the former Women Medical Specialist Corps, she had served in the Medical Department of the Army as a civilian. She is the immediate past president of the American Occupational Therapy Association.



Colonel Robinson



**CAIRO CEREMONY** Captain John R. Seal, MC, USN (left), commanding officer of the Naval Medical Research Unit No. 3, Cairo, Egypt, who hosted a reception hour recently to the Honorable Raymond A. Hare, United States Ambassador to the United Arab Republic, and Dr. Nur el Din Tarraf (right), chairman of the Executive Council, Egyptian Republic, on the occasion of the tenth anniversary of the founding of the laboratory. More than 400 guests attended the ceremony.



**GENERAL OGLE DECORATED** The retiring Surgeon General Air Force Major General Dan C. Ogle (right) is shown receiving the Distinguished Service Medal in a Pentagon ceremony recently. General Thomas D. White, USAF, chief of staff of the Air Force, is exceptionally meritorious service to the United States in a position of great responsibility. General Ogle, who retired on 30 November, has been succeeded by Major General Oliver K. Niess.

## USAF COMMAND DENTAL SURGEONS MEET

Major General Olin F. McIlhenny, Deputy Air Force Surgeon General, gave the welcoming address at the annual conference of the Air Force command dental surgeons in Washington in mid-October. The conference was conducted by Brigadier General James S. Cathro, Assistant for Dental Services, to discuss the policies and procedures affecting dental service operations at command and base level. Procedures for increasing the effectiveness of current education, preventive dentistry, and research programs were discussed. Colonel Donald C. Hudson, chief of the Research Dentistry Division, Randolph Air Force Base, Texas, presented the results of investigation of ultra-high speed handpieces and auxiliary equipment for cavity preparation and these were recommended for all Air Force dental clinics.

## Official Decorations

The following awards were recently announced by the Departments of the Army and the Air Force

### Distinguished Service Medal

D C Ogl M I G USAF (MC)

### Army Commendation Ribbon

Glb t M E C pt. USA MC Ch l L Glb C l USA (MSC)

### Air Force Commendation Medal

J hn F P Lt C l USAF (MSC) F d k S. Sp g l Lt C l USAF (MSC)  
J h M R g Lt C l USAF (MSC)

W h m l p da

## DEATHS

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## CORRECTION

The n w address for Brigadier Gen l Thom s W M ttingly MC  
USA (Ret) w s i co ectly g v n the September *Jo rnal Dr M t*  
ti gly i th D ctor of Med c l Educat on f the W h ngton Ho pital  
C t 110 I ng Street N W Washington D C

## A MESSAGE FROM THE A M A

In October 1958 the Committee on Military Medical Affairs, one of the two Committees of the American Medical Association's Council on National Defense, met with the Assistant Secretary of Defense (Health and Medical) and his staff and the Director of the Selective Service System in regard to matters of mutual interest to the military services and American medicine.

One of the topics discussed was the expiration on 30 June 1959 of the Universal Military Training and Service Act of 1948, as amended. While every registrant who has been deferred has a general liability until he is 35 years old, irrespective of the expiration of the Act, the authority to induct registrants who have not been deferred would terminate if the Act is not extended.

Under the present amendment to the basic Act, which became effective 1 July 1957, the Department of Defense has been able to fill its requirements for medical officers from volunteers. The last draft call for physicians was in February 1957. Since that time, however, there has been a steady decline in the number of interns volunteering for deferment and subsequent active duty in the Armed Forces Reserve Medical Officer Commissioning and Residency Consideration Program, popularly known as the Berry Plan. This decline may be due to the fact that the young medical school graduate is aware that there is only one chance in two of having to serve, so he takes a chance on not being called.

Unless renewed interest in the Berry Plan is shown by interns, it now appears that a draft call for physicians will be necessary in fiscal year 1960 if the military services are to fulfill requirements for qualified medical officers.

Any extension of the general draft law, including the special provisions for the call up of physicians, will be considered by the 86th Congress which convenes next month. It appears that the Department of Defense and the Selective Service System will propose that the draft law be extended beyond its expiration date of 30 June 1959 in substantially its present form. It is believed that the obligation to serve which the law provides, is necessary if the needs of the military services for medical officers are to be met by volunteers or otherwise.

With respect to the extension of the special provisions of the draft Act applicable to medical, dental, or allied specialists, the American Medical Association has recommended that the Act not be extended beyond its expiration date. The Association

From the Council on National Defense of the American Medical Association. The new deadline expires does not necessarily those of the Department of Defense.

believes however that if the demands for the defense and security of our nation are such that in the opinion of the Congress it is necessary to have a draft act to maintain the strength of our Armed Forces then the extension of the present legislation would be one method to ensure sufficient physicians for the military services This is a reaffirmation of the policy position of the Association which was adopted at the time the present amendment to the basic Act was proposed

The Association also has recommended that there be retained the provisions of the law relating to the National Advisory Committee and the local and state committees which advise the Selective Service System in regard to the selection of needed medical dental and allied specialists required for service These committees consider among other factors the needs of the civilian population in the communities from which the physicians would be taken

In regard to specialist categories moreover the Association recommends as it has on a previous occasion that the word other should be substituted for the word allied wherever it appears in the law This would authorize a selective call for all other specialists such as engineers mathematicians physicists et cetera needed by the military forces Presently the law provides for the selective call up of medical dental or allied specialists

The Association believes that physicians should be registered and classified in the same manner as other citizens in the same age group deferred for educational purposes in the same manner as other registrants and called to active duty or inducted under the same general provisions as other registrants deferred for educational purposes

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## Major Anthony Borski Wins Kimbrough Award

Major Anthony A. Borski, MC USA, Fitzsimons Army Hospital, Denver, Colorado, received the James C. Kimbrough Memorial Award for his presentations on Evaluation of Renal Function Using Radioiodine Diodrast and Genitourinary Tuberculosis at the annual urologic symposium in honor of the late distinguished Army urologist held at Brooke Army Hospital, San Antonio, Texas, 3-5 November. The award consists of an honorarium for urological public relations, the gift of Mr. Kimbrough, the ten-volume program of scientific papers and case reports was arranged by Colonel Louis K. Mantel, MC USA, Chief of the Urological Service at the hospital.

# OFFICERS CERTIFIED BY SPECIALTY BOARDS

The Surgeons General of the military departments have announced certification by specialty boards of the following officers of the regular establishment since publication of listings in previous issues of the *Journal*

## American Board of Psychiatry and Neurology

### *Neurology*

Henry W Hoga M J USA

## American Board of Orthopedic Surgery

P l W Br wn M J USA

## American Board of Urology

W l l m A C l l i Jr Lt C l USA S m l R drig ez Lt C l USA

## American Board of Internal Medicine

### *Gastroenterology*

N rm M Sc tt Jr Lt Col USA

## American Board of Pathology

### *Pathologic Anatomy*

Pr ct r L Ch ld M J USA

R b rt S C Jr C pt USA

J m L H s Lt C l USA

J me C H yes M J USA

P l W Palmer M J USA

### *Clinical Pathology*

R b rt S Co J Capt USA

## American Board of Otolaryngology

H rry W McCurdy M J USA

## American Board of Surgery

H A Bl k Lt C l USA

Ol r R Bues g Lt Col USA

R bert D P l l bury Lt Col USA

Don ld W Robin o Cd USN

J k T R h Lt C l USA

## American Board of Oral Surgery

L kor h Lt Col USA

## American Board of Prosthodontics

J hn F B wma Capt USN

F nk J Kr t ch il Cd USN

Chr stoph r E Thomlins Jr Capt USN

## American Board of Veterinary Public Health

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A L K A L E S C E N S - D I S P A R 01  
h g l l l k i t r m e d t s r o t y p e i n  
d y s t r y p d e m i c 965

## ALKALOID

p e d r f o r d t e c t i o n o f 845

## ALKAPTONURIA

c 911

t t s f d t e c t o f 912

## ALKYLATING AGENTS

t r m t f d s 795

t r g e n m t a r d i c n e r f l g

o r y n d b e 799

t g m t r d H o d g k s d e  
799

t t h y l a m e l m s d C a B s 1348  
(L e u k s ) a c h o

## ALCOHOL

r e s e a r c h o f

F a r d e r s s

A l c o h o l c o n t a i n e d i n f i n a

A l c o h o l

C o l o r a d o c o n t a i n e d i n f i n a

185

A l c o h o l c o n t a i n e d i n f i n a

F a r d e r s s c o n t a i n e d i n f i n a

185

A l c o h o l c o n t a i n e d i n f i n a

t r a n s f e r o f c a r e l l w a r d s

t r a n s f e r o f c a r e l l w a r d s

A l c o h o l c o n t a i n e d i n f i n a

a n d t r a n s f e r o f c a r e l l w a r d s

185

E u r o p e a n f i n a n c i a l r e s e a r c h

m o n e y d e n o t i f i c a t i o n o f A r

201

C o m m u n i c a t i o n s t y m t f a l l i n

n e w s p a p e r s a n d m a g a z i n e s

C o m m u n i c a t i o n s t y m t f a l l i n

n e w s p a p e r s a n d m a g a z i n e s

185

C a l i f o r n i a f i n a n c i a l r e s e a r c h

m o n e y d e n o t i f i c a t i o n o f A r

M e d i c a l A l c o h o l i n f i n a

n e w s p a p e r s a n d m a g a z i n e s

m o n e y d e n o t i f i c a t i o n o f A r

S u r v e y o f f i n a n c i a l r e s e a r c h

i n t h e U n i t e d S t a t e s

t h e A l c o h o l i n f i n a

C a l i f o r n i a f i n a n c i a l r e s e a r c h

m o n e y d e n o t i f i c a t i o n o f A r

R e s e a r c h o f f i n a n c i a l r e s e a r c h

A l c o h o l c o n t a i n e d i n f i n a

A l c o h o l c o n t a i n e d i n f i n a

A l c o h o l c o n t a i n e d i n f i n a

185

A l c o h o l

n e w s p a p e r s a n d m a g a z i n e s

185

A l c o h o l c o n t a i n e d i n f i n a

n e w s p a p e r s a n d m a g a z i n e s

185

A l c o h o l c o n t a i n e d i n f i n a

A l c o h o l c o n t a i n e d i n f i n a

A l c o h o l c o n t a i n e d i n f i n a

A l c o h o l c o n t a i n e d i n f i n a

A l c o h o l c o n t a i n e d i n f i n a

A l c o h o l c o n t a i n e d i n f i n a

A l c o h o l c o n t a i n e d i n f i n a

A l c o h o l c o n t a i n e d i n f i n a

A l c o h o l c o n t a i n e d i n f i n a

A l c o h o l c o n t a i n e d i n f i n a

A l c o h o l c o n t a i n e d i n f i n a



## ANEURYSM

d g bd m l (CPC) 399

ANIMALS S und p f e am f

m l Dog R bb R d

ANOMALIES. S Abn m l und

m f p f g

ANTIBIOTICS S l d sp f

m Ery h my O y y l

p ll S p my

d dur g l g q m f

d 370

p dem f fl d fl a-

l k sy d m 479 495

m ddle ar f 1426 1432

## ANTIPERSPIRANT

d ph m l m thyl lf l nu l

f 177

## ANXIETY

d g f m h 1190

## AORTA

bd m l d ct g ry m (CPC)

399

APC POWDER (A tyl l cyl A d

A ph d and C ff )

d Aur my h p p

f l l fl 479

APPARATUS S l P h

B w eu m cul ul

g GB po so d d g

( p d ) 600

m k l r fl g d l p d

by A my Ch m l C rp 1227

m d l lf l g 983

xys d p h urg y

1119

pl i d l f l pl

39

pp m in fun l foo

p B k si 817

urn q ll w d-B ley p eum

l 94

## APPENDICITIS

m und subop m l

d 1545

## ARMED FORCES INSTITUTE OF

## PATHOLOGY

f d f l l f

p b l g g g 207

nn un V ch w en l l ctur

1524

## AR IS T R O N G H A R R Y G

l d d p m d

1376

uc d d b G al Tw h ll

USAFE urg 124

## ARMY

d l l 811

pp d ur m nd

bop m l d 1545

l bo ry l ky 843

## ARMY (Co d)

A m g ll ry G f m Surg

G l 1376

A ll F B l Va.

802

B J ph L m d and g

d 1380

B k A h y A p d J C.

K mb gh M m l Aw d 1806

Ch m l C rp d l p w typ f

l r flt g m k 1227

h ld gud l 1161

C l w l f d l

w k 1298

l l d p g

180

C f d d h d dy en y

1780

C f d m d l ff h

f fd 1580

l d h p l mma d

m F G g M d 1222

d sh pm f book h 593

ph g l by emp d

d 728

H y l Ch f f A my Nur C p

J p 1665

fl p dem F et D 469

479 487

l w Army H p l m d h f

G l w 761

K mb gh U l g l Sem h ld

W l R ed 126

L man J th d d gh er

l F b

M Army H p l d d ed 1217

M A my H p l F Benn g

G d d ry ddr 1168

M d l R h d D l pm

C mm d w h ad d by J ph H

M N b 1670

M d l R d ry g oup m

751 ( ) 1065

m d l d d f f ll m b l

1605

w h ep l d d d t Ok naw

1224

N l C l A p f

m gl 450

er B ard Aw d 449

ur d C l W p d, 1310

p g d p f l ur

ff d A my M d l Ser ff er

754 1070 1672

R b R h A m d f ur h h f

f M d l Sp l C p 1802

Sayd Ag P l d pr d f

Amer Phy l Th py A a-

1226

T pl Army H p l ry

1522



## AWARDS (C i d)

Ly Th d C. Aw d p d

H b S gh ld 590

M L waded Wll m H

L wt 1798

m d l w g w d o f 593

M d m Med l M g ph Aw d

f 593

M l y H ry G p en f Raym d

F L g Aw d 590

M l f Om h P bl S Award

d by C l S pp 286

N vy D g h d C l Aw d p e

d Cl y G H ff 760

N vy C f f M p d

CIBA Ph m l C mpany 752

S M j L L g

P g R ll L B h p

1798

S Aw d p d C g L

C l y 1798

S gh ld H b Th d

C L y er Aw d 590

T t l Am ld D Aw d p en d to

S g f d j G th h l 590

W k L B E g l

P B d Aw d 449

W ll m S H y M d l nd P

w d d Cal W H gh 1728

## BANTZ, FRED A.

A S ry f th N y p e

N vy Cet f f M

M T F D H 752

A S ry f h N vy p e

D Cl y G Huff w b N vy

D g h d C l Aw d 760

## BARBITURATES

p d f d f f 847

## BARR NORMAN L

d d g d f f ll w A

M d l A 590

## BATROW NEUROMUSCULAR STIMULATOR

g GB-r d d g

( p d ) 600

## BAUCHSPIES ROLLIN L

g h M l L g

Se m P 1798

## BAUER LOUIS H.

y-g er l f MA mm

d l c ld fen emblem f w ld-

d 1522

## BENFORD ROBERT J

d B nn F A ery d f

l S A med F M d l j urnal

1522

## BERNIER JOSEPH L

m d st d g den 1380

## BERRY FRANK B

g en F h A t d ll d H nn ur

## BERRY FRANK B (C t d)

d S d S en O P

m y 914

g h ry f ll w h p l

l C ll g f D t 129

g m g f R C l

B d Bur f M d and Surg ry

N y 1219

h Turk h h A k 914

Wh H c em y mak g

P d E h w h ary f ll w

f Am C ll g f Surgeo 588

## BEYVE J P

p d f A f M l ary

S g f F 914

## BILLROTH CHRISTIAN ALBERT THEODOR

D B g mp f 654

## BIOLOGICAL FLUIDS

g b mid p d d mpl

p dur f d f 498

## BLADES BRIAN

Wh H us m y k g

P d E h w h ry

f ll w f Ame C ll g f

S g 588

## BLEEDING S Blood

## BLOCKER TRUMAN G J

onf f Ad ry Coun l

R Aff 751 ( )

1065

## BLOOD

b c blood f

l gur p 370

bl d g ph g l w h

m g l b m b g

(CPC) 1176

bl ed g g l nd l f lur

(CPC) 891

h l st l d m nat f 501

h l t l hyp h l m d

hyp l p m us f h m

d b m 268

ff f d 1705

h m gl b d mu p p l

f f d d d 684

hype al m us f EDTA 989

hyp l p m l 1414

l p d nd homa d b um 268

l p d se l hyp l p m 1414

l yt d h m gl b C

1370

pl ma p ur d pool d h m

l l l f 1249

p m hyp k l m f m l d

p m d pl (CPC)

533

m bl b nal

h p t dy f 1201

lum ed p rt f m k g

f m by 1456



## DEFENSE

A ry B F ppo ed l  
 oodm f M die l Ed f  
 N l D f f gram 1522  
 l f m l ry rv 1668  
 m d l l mbl m f wo l d w d  
 1522  
 m b l t o o med l andard f  
 1605  
 na l al ctiv f A M, A 1520  
 N na l l d partm Comm tr  
 N f m k ur y N  
 and F E 91

d GUTIERREZ-MAHONEY CARLOS G

l l Surgeo G l  
 f A F USAF 920

## DENTAL ADVISORY COMMITTEE

fun f f Jan

DENTAL CORPS OFFICERS S M d  
 l Off D ry

## DENTISTRY

As F mm d den l urg  
 m 1803  
 Am an D l A oc p d  
 m U S, and J pan d l  
 ff dur g p Far E 1066  
 an th i i loc l 625  
 B r n J ph L m d and g  
 den 1380  
 Bod Ry L l c d p d f  
 h Ac d my f Impl D ur 129  
 Ca hroe B g G w A an f  
 D al Serv USAF 398 591  
 D l Ad ry Comm f Jan

den l d d ry eten  
 andard m l ary rv  
 1636

D l Co p ff rt f d by pe-  
 lry board 133 594 919 1069  
 1225 1380 1807

D l Co p ff d th f Se  
 D h

D l Co p ff ga  
 f f Mar h

l l Coll g f D h ld  
 m g in R m 129

h b k Mar E A an f  
 Den l Serv Off f A F

Surg G l L g f  
 M 591

M l Ralph W h f f N vy  
 d l di 1800

marro ff-cl an g 983

Sch Curt W h f f N vy  
 d ld 1800

Sch Curt W l cted f p o-  
 m ar dm l 1377

l d l f l pl

## DEPARTMENT OF DEFENSE

A m d F E m g S d  
 m l m l d phy l andard  
 f g an 1606  
 Arm d F Sp l W po P l ct  
 M d l Symp uma f 1380  
 B ry F ank B d ff and D  
 f S l S rv Sy mm w b  
 AMA Comm Mil ary Med l  
 Aff ur 1805  
 lan med l lan g d by  
 P d E h w 123  
 D l Ad ry Comm i f j

D p d M d ar P g m, ed  
 1405

m d l ymp um Sand B  
 N w M 451

m mb f C l Ad ry Coun l  
 f and M d l Ad ory Coun l f

C d D partm f N l De-  
 f f j ly

M l ary As Ad y G p  
 w k l g m d ll f

N mb  
 rv m d l un 1668

U.S. Arm d F M d l j ur l  
 k lan ed 1068

DEPENDENTS MEDICAL CARE PRO-  
GRAM

ff p m ed t b g d  
 g l 1666

d 1405  
 R b P l l E ut D ct

1378  
 W g land Fl yd L w E

D 1378

## DERMATITIS

h p f m und 11 y ar f  
 in tr m w h lf pyr

d 907

## DERMATOMYOSITIS

ed w h p g ancy 417

## DIABETES

k w h tran i l ff  
 y 1351

## DIABETES MELLITUS

d m l g man f f 1654  
 b l po d di b i rum

1654  
 an h m d be ocum m f a-  
 f 268

## DIAPHRAGM

H S H rn Morg ga 187  
 h rn lf ded uma l g

ld 1204

## DIARRHEA

fff h tumn B l f G ry borg  
 1779



## DEFENSE

A y B F ppo ed l  
d f M d l Ed f  
N l D f p gram 1522  
l f m l ry rv 1668  
m d l l mbl m f w l d w d  
1522  
m bil ti m di l and d f  
1605  
na l al ct it f A M. A. 1520  
N na l l d partm t Comm  
N f i m k ur y i N  
d F E 91

d GUTIERREZ-MAHONEY CARLOS G

f f Surg G l  
f A F i USAFE 920

DENTAL ADVISORY COMMITTEE

fun f f Jan i

DENTAL CORPS OFFICERS S M d

e l Off D ry

DENTISTRY

As F mm d den l surg  
m t 1803  
Am D l A p d  
m t U S. and J p d l  
ff c d g p Far E 1066  
an th jet i c l l 625  
B J ph L n m d d g  
dent 1380  
B d Roy L l d p ld f  
b Ac d my f Implan D ur 129  
Ca h B g G w A l an f  
D l Serv USAF 398 591  
D l Ad y Comm f Jan

d l d ad y  
dard mil y rv

1636

D t l Co p ff r f d by p  
lry b d 133 594 919 1069

1225 1380 1807

D l Co p ff d th f Se

D h

D l C p ff g e

f f Mar h

l l Coll g f D b ld  
m g in R m 129

K b k Mar E A an f

Den l Serv Off f Au F  
Surg G l L g f

M 591

M l R lph W b f f N vy  
d l d ur 1800

m lf-cl an g 983

Sch C rt W b f f N vy  
d l d 1800

Sch Curt W l cted f f p o-  
mo dm l 1377

pl d f f l pl

39

## DEPARTMENT OF DEFENSE

Arm d F E m g S t and  
m l m l and phy l ndards  
f t g 1606  
Arm d F Sp l W po P j  
M d l Symp m t f 1380  
B y F k B d ff and D  
f S l c i S rvc Syt mm t w h  
AMA Comm Mil ary M d l  
Aff 1805  
l an m d l l g d by  
P d E h w 123  
D l Ad ry Commi i f j

D p d M d P g m d  
1405

m d l symp um Sand B

New M 451

m mb f C l Ad y Coun ll

f d M d l Ad ry Coun l f

C d D partm t f N l De-

f j l j ly i

Mil ary As an Ad y G o p

w k l g m d ll i f

N mbe

rv m d l un 1668

US Arm d F a M d l j r r l  
k l an d l 1068

DEPENDENTS MEDICAL CARE PRO-  
GRAM

ff p m d b g d  
a l 1666

d 1405

R b P l l E ut D

1378

W g land Fl yd L w E

D 1378

## DERMATITIS

b p f m s und 11 y ar f  
tuno tr m w h lf py

d 907

## DERMATOMYOSITIS

s t d w h p g ancy 417

## DIABETES

ke w h ur l H

c n y 1351

## DIABETES MELLITUS

d m l g m f t f 1654

cr b l po d d b um

1654

b m d b um m f

f 268

## DIAPHRAGM

H m S H m M g gni 187

b m l f ded una in l g

l d 1204

## DIARRHEA

f f h lunn B l f G rty burg

1779

## FOOT

flatf ot d try or s t ti n stand  
d in m l tary s rvi 1615  
myc tom p di c s pot emph  
ing rad g phic ch g s 577  
pp rt to ma nt funct o l p it n  
f n B ck te 817  
v tr a pl ari u f p l lary tub  
g fo applyi g acid 972

## FRACTURES

comp o f ert b t d by  
mm d te p og m b liz t  
1736  
f p r t b n 1513  
k ll d pr s d r p of cran l d  
f ts f ll w g 375

## FRANK WILLIAM B

d d t c m f l  
t l ho p t l 125

## FREEMAN PAUL L JR

pr t k yt M rt Amy H p r l  
t C l Sk 1217

## GALACTOSEMIA

g t l 112

## GALLOFAY CALVIN B

l t d f pr m t nt d m l  
1377

## GANGRENE

f p p c f ll w g l l ane th  
120

## GARDNER CLARENCE E JR

p p l p ak C mb land Coun y  
Med l So ty m t g 287

## GAS

m t d d m t d l k c mpound  
t m t f d e 795  
rv f B tr w ur mu l  
s m l t r f d c ng pr  
n m l pos d w b (c e p d  
ce) 600

## GASTROINTESTINAL TRACT

d and try r t t t d  
d m l t ry 1622  
dy t ry f f b l m arm f  
h p t 1779  
m l pl ty f c r t l s ( d i  
t al) 447

## GENITOURINARY TRACT

m f rv 1444  
d f d y t  
d d m l tary rv e 1627  
ur l p y ung g l 1213  
ur ry d ur t l  
ct r 1213

## GERATHEWOHL SIEGFRIED J

p f Ar l d T t l Award  
590

## GLOMERULONEPHRITIS

c t d f f s h m h g t (CPC) 1785  
b c t (CPC) 891

## GLOVE

c m ti fo pro th t c h d W lter  
Re d ch r l tr p te t  
for 450

## GOITER

d lar 1558  
t i w th thy d c c s s a d g  
ul yt p 571

## GORBY EARL W

r p nt of H f f M d l 1224

## GRAFTS

ant t s l b i p r o f c r i l  
def c r s 375  
bo g l t r p l c m t i m o t t i c  
P g t s d fat f 1508  
spl t k i p m ry t r t m t o f  
larg p l d l c y s t 957

## GRANULOCYTOPENIA

and thyr ard c c r i s p t t w th  
thyr to s 571  
f ll wing ther py w th pr pylthi racil  
571

## GRAYBIEL ASHTON

d c t c t t s o f m t i n g o f A r o  
M d l A c t 590  
p s d nt f A M d l A s i t i o n  
443

## GREEN GEORGE B

w Found M d l 1799

## GRILLS HERBERT L

w l m g t t d d c t i o f  
L k l d A Fo B e h p r l 132

## GUNER TEVFIK

Surge G l f t r k i s h A r m d  
F c s d F a n k B B r y h o n r  
T k h h r A k 914

## GUTTMACHER MANFORD S

tt d m et g f A m y c l t t a  
d b p t i c m m a d 1222

## HAGERTY JAMES C

pe k r t m t g o f l n m d i  
l t n t 123

## HAIR

l f w h e n c d b y p e t r t r  
n g r d t 347

## HAITI

U ty f l l a t D e n t l S c h o l r n m  
12 t t n d g d t f r h l  
1380

## HANDS

ps d w l l i n g p e b o  
d 277

## HANSON LAWRENCE B

arra g p r s m c f m e d i c l s y m  
Ca dia B



## HARF RAYMOND A

U S Amb dor d ha s f  
mmand m l m d cal

h un t Cair Egypt 1065

U S Amb d U t d Ar b R p b  
l g t N l Med l R ar h

U N 3 C ur Egypt 1802

## HAYNES INFZ

Ch f f Army Nur Corp

J p 1665

## HAYS SILAS B

t f f Ad ry Coun l on

R rv Aff ur 751 ( t ) 1065

## HEARING

l d po ur h gh ty  
1038

l f ll wing nad qua tr m f  
ot i m d 1425

## HEART

an m l manag men fl pr bl m

f ll wing p d tr urg ry 1155

an ry d ar ng f m

1190

d in h ma f 1437

g l d f pulmon ry lar

h g in 1132

ary ry oc lu on y m

loc lf or in 12

d l d hypertr phy w h myoc d l

f lur (CPC) 255

d d d try or on d-

ard m l ry ry 1617

f lur (CPC) 1639

f lur nd do ard l l b oel

f (CPC) 1319

f lur g t f d rained

us 438

f be l d ard l with my

rd f f lur in afan (CPC) 1319

p h rt urg ry xtr po l t

ult f 1119

pain f tal had wed by p y ho-

g man f 1184

pa pe ult c ing inf

f p y hon ur 1184

pe of f y d d rt f 1448

pe d t p d ng l f ga

f p umococ l p um 1359

f pulmon ry and tr c p d

l d m ll gh l pul

m ry ular chang w b 1132

hyoc rd and granulocyte

in pa t w th hyr tox f 571

## HEATON LEONARD D

in pe f l iter pa Cal

A N l on 450

Th H us m ymak g P

d E b w b oary f ll w f

Am Coll g f Surg 588

b or ry d gt f Doc f

## LEONARD D HEATON (C d)

Sc fr m D on Uni ry

1064

## HEAT STROKE

d ml rype no l 1106

lin lf ur f 1112

l b ry f d ng in 1114

path phy l gy 1107

w f b 1001

## HELICOPTER se Airc f

## HEMOGLOBIN

C tr d locyt 1370

bl od lw y true ind f

tot l m un f h m gl bin 1436

pr po lf rt f d andard 683

## HEMOGLOBINOMETRY

t f d dard f us in 683

## HEMORRHAGE

ga tr in l m w h bl d

g ph g l ar (CPC) 1176

rapulm nary (CPC) 1639

W ll be g yud m ul g 1364

## HEMOTHORAX

arly lot d lum d thor omy nd

ym t b py in 949

## HEPATIC DYSFUNCTION

t l f m ly 1198

## HEPATOMEGALY

d f (CPC) 1176

## HEPATOSPLENOMEGALY

l hype l pem 1418

## HERNIA

d ph gm tu lf d d tr um

in l ung l d 1204

ph g l h l d w b

h rn f M gag 187

f bd min l ty and try

nd rd in m l ary 1622

f M g g oc ed w h ph g l

h l h rn 187

## HILLEMAN M R

d m ing f Army ul

and h p l mma d 1222

## HISTOPLASMIN

kin p pe d

ha g ub ul 885

## HISTORICAL ITEMS

B l l e b Chr Alb rt Th od m

m oo ing 654

Camp B aning G mm arly

day f 1168

C l War d arrb and dy ry

1780

C l W r h p l or 1305

C l War l f rv 1298

C l W oc al w k 1298

C l d ra Army di rh and dy

tery in 1780

Conf d rat m d l f in h f l d

1580

## HISTORICAL ITEMS (Continued)

d n t tstanding of U S in photo  
gr ph e hub t in Hatt, 1380  
di rth f th olmn at B tle of  
G try burg 1779  
dy t ry in rmi f th past 1779  
G tryburg fifth c lmn t B tle of  
1779  
Infirmary Corp in Confedera Army  
1585  
Irwin Bernard J hn Dowling for whom  
Irwin Army H pital wa named 761  
Lett rman Jon than and da ghter of  
of F b u  
M rtin J ph I comment ou 1169  
ur s in C l War per od 1310  
O l William omm nt c ng  
662 1174  
P st ur L uis ommnt con ern ng  
657  
per alti s d epochal event in  
md in 654  
pr ts f Co f d t ad U n  
m s tr m t of 1594  
h f s rv forth C l W sold  
1298  
R t P val She er form Sur  
g G l U S N vy d 282  
urg o s C l War cha g of 1595  
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1588 1591  
U S S t ry Comm d p l  
l f d partm t 1300 1302  
Wh t H doct r 595 ( or pond  
) 1383

## HODGKIN S DISEASE

tr g m stard in tre tm t f 799

## HOGAN BARTHOLOMEW

nd st f d sc s N vy Gr duat  
M d c l T g Progr m w th R  
e C l t t Bo d 1219  
acd d t on c mon f l u t  
cl r r t r t l l d s b p t l 125  
t p t t f N vy Certif t f  
M t to CIBA Pha m c t c l C m  
pa y 752  
g p t ud c with P p P u  
XII Eur pe t ur 1218  
on t ur f N vy m d c l f cilt t  
N pl s 915

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m l r p

## HOSAKA TSUNEO

Ch f D t l Off f j pa Self  
D f F d b q t t  
b t f W l l m R Alt d 1066

## HOWARD WILLIAM A

l l ry f l med c l  
l g r 123

## HUDSON DONALD C.

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ultra high speed handpieces at dental  
c nf nce 1803

## HUFF CLAY G

pr nt d N Vy Di t nguished Civilian  
Award 760

## HUGHES CARL W

win Sir Henry W l l om M dal and  
P iz 1798

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d coma f llowing o e dose of  
mep b m t 1692 1698

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g t A l l e z n N y f  
fic y f 1720

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tom poss bly r l t d t 1659

t quirem t f tr el ts informa  
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ma (CPC) 1049

## INFANTS (Co d)

M k l d rt ulun 1049  
M k l d lum pe for d 1505  
m ph l d f us papyr  
1007

pulm ry ular h g ong  
l b art d 1132  
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b m g us my l t i 1336  
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hr mb phl b d b l  
my l in 1336

## INFLUENZA Se l R p ry Sy

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A valua f in b k f  
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## INSECTICIDES

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## INTERDEPARTMENTAL COMMITTEE ON

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IRAN

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d f (CPC) 690

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1648

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Air F B 1801

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 c se 57  
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## LONG PERRIN H.

pr id f en f Ad ry  
C un l R erv Affair 751 ( ) 1065

## LOVEJOY F D

b ary d g f p

1671

## LUETH HAROLD C.

f f Ad ry Coun l on  
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## LUNGS

l f l and mphy m  
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omp rim ur fl w b ru  
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f f 1759

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ular hang w b ong l h ar  
di 1132

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po to urh m nk f 426

## LYONS JOHN H.

in Wh H us mony m k g P  
d E enh wer h ary f ll w f  
Am l an Coll g f Surgeo s, 588

## MALARIA

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g oop th f ld 1753

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ur ly 1757

## MALATHION

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us f m l d 273

## MALONE RALPH W

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## MALPRACTICE

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ng p gr m f en f p p

and po f an l ur l g l  
m 1806

## MARBLE ALEXANDER

f Ad sory Coun l

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## MARGARIA RODOLFO

pr f ur h L ui H. B l

ur 443

## MARINE CORPS

Mar P M b w j M K and  
ff f f Jun

## MARINE CORPS (Co d)

pr f war den f b

ul m g 882

ub ul p d m l g udy f  
705 872

## MARSHALL LESLIE B

w b f f publ on di

Bur (M d and Surg ry N vy  
1522

## MARTIN JOSEPH I

br dedi ry pl q un led by

Mr Martin 1217

m 1169

w h p l t F t B g G

m d h bo or 1168 1217

## MASK

l ur fl g d l p d by

Army Ch m al C p 1227

## MASON JAMES B

f f Ad isory Coun l

R rv Aff u 751 ( or ect on) 1065

## MATTINGLY THOMAS W

ur 1378 ( r on) 1804

## MAXWELL EARL

ur 1518

## McCONVILLE JOHN

y ung p t U S. Army Med l

Cen ) p gr et d by Army h l  
ur 1665

## McGIBONY JAMES T

mmander f w h p lo Oki w

and urg U.S. Army Ryuky

ll d 1224

## MILNAY OLIN F

d d w h p l A dr w Ai

F B 1801

g w l ou g ddr t an ual

f f Air For mm d d l  
urgeo 1803

## McKAY JOHN A.

t Cumb l d County M d c l So ry

m g 287

## M MAHON ALPHONSE

l d h man f A.M.A. Se i o

M l ry Med 1377

## M NINCH JOSEPH H.

b d Army Med al R ar h d

D l pm C mma d 1670

## MECKEL S DIVERTICULUM

mpl f 195

2 m h ld infan (CPC) 1049

perfor d in 3-mo h ld inf 1505

## MEDIASTINUM

m imul d by al phl b

901

## MEDICAL EDUCATION WEEK

601

## MEDICAL OFFICERS

A F ff et h en pr d

l f Am i Coll g f P

## MEDICAL OFFICERS (Continued)

t e Med n 281  
 Amer c n M di al As oc tion Servi  
 Memb h p in 444  
 Award S Award  
 Certif ed by Sp lty B ard Se  
 Sp c lty B ard  
 C f d rat in th fi ld 1580  
 credent l medical cnt l epo t ry  
 f 919  
 dr ft l w AMA vi w n rn g 1805  
 dut n cl ar subma in 867  
 D ath Se Dea h  
 D at Se D t n ff l  
 h t to Cumberla d County Med cal  
 Soci ty meet g 287  
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 p th l g st erv f 209  
 po tg dua pr f on l ur f  
 f d 1070 1672  
 P m t Se P mo on  
 l d f m ct military rv  
 p nt urv y am ng 597 757  
 r rv c ld fen 1668  
 gn t f f Mar h  
 Surgeo xchang f during Cs l  
 W 1595  
 Wh H doct (editor l) 595  
 (c pond ) 1383

## MEDICAL SERVICE CORPS

Army ff f ffered po tgr duat  
 p f l our 754 1070 1672  
 ff c d h of Se D h

## MEDICAL SPECIALIST CORPS

A my R th A R b m d h f  
 f 1802

## MEDICAL STANDARDS

f entry d etent m lta y  
 c s 1605  
 f r f l m b l z a t o 1605

## MEDICINE AND THE LAW

b l g c l s p c m e n s h p m in  
 m d c l g l c 844  
 c m p e t c p ry tud  
 p u t b g d d 1286  
 m l p d h ervic d 224  
 c l g m nat on and d t rm  
 t s p f med in g t  
 med c l g l s 845

MEDICOLEGAL Se Med and h  
 L w

## MEETINGS

Ad ry Coun l R Aff  
 Surgeo Gen l Army 751 ( r c  
 ) 1065  
 A ro Med l A oc t 443 590  
 A For mm d d t l ur g  
 l f en f 1803  
 A h l gy R w Se on f  
 Arm d For f 915

## MEETINGS (Continued)

Arm d F Medical sympo r m a  
 Sand Base N w Mex.co 451  
 Arm d F Sp c l Wea, o s P i ct  
 M di l Sympos ums tuc of l  
 As i tion of Military Surgeo s  
 w rd p sented t 1798  
 A soc ti f M l tary Surg us t ce  
 f 1667  
 t m weapon m d l asp cts of  
 sympo m 1380  
 Cs l M dical Con ultant to A.m d  
 F 123  
 Cumb land County Medic l Soc ry 237  
 K mbr ough U log c l Seminar held t  
 W lt R d 126  
 N t nal C f en Air P ller  
 t c f 1667  
 NATO Mil tary Medi l Conferen  
 f Aug t  
 P g p b l m discu d t 1798  
 symp m n t x h zard in \*  
 t 287  
 Tw lfth Int rn t n l Dental Cong. t  
 h ld R m 129  
 W ld C gr s f A t n M d ne,  
 1221  
 W ld H lth As mbly WHO to meet  
 U S 756

## MELIOIDOSIS

t f 273  
 MELOY GUY S.

pr ent Elb rt DeC ur y h the rns  
 f m l gen r l 1666

## MENINGOENCEPHALITIS

t l g c s t 1281  
 virol g d gn t c m thod 1282  
 MENTAL HEALTH Se lso ad  
 P y h l gy d Psy h try  
 Coun l r pot on m d  
 hyp 1381

## MEPROBAMATE

P tyl t r x l (M t x ) s  
 t 1700  
 sus d t m p s w th l / 2  
 t c ty 1691

METHODS Se l s T h  
 p d m l g c a d y of A  
 N vy d M n C t r y  
 b l f nd s t

## METICORTEN Se P l l

## METRAZOL Se Pentylm

## MICROCOCCUS

ant b t i ant ant p  
 p t 161  
 pyos va wren at  
 t d to and broad  
 (CPC), 1785  
 pyos var wren.  
 gen o comp etit

## MICROCOCCUS (C ti d)

p m ling from 1336  
py g ur us pharyng 1  
b d (CPC) 1049

## MILITARY MEDICINE Se l As

F Army D partm f D f

N vy

A M A Se l D Alph  
M M b h rm 1377  
m lua f in b g m d l

p cti 21  
ur W l R d Army Ia

f R ar h, 290

d arch dy ery f f b lumn

arm f th pa 1779

b k 1106

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1605

pl urgery l 1146

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l b um f in m l ary p so l

1436

k ll ll d p y h udy

f m l y p sonn l 1745

Turk y p d m f b l pl ur y w h

ff in l

## MILLER ROBERT R

pp d A au f V ary Ser

Off f A F Surg

G l 130

## MIRROR

d l ll l aning 983

## MOBILIZATION

full m d al standard for 1605

## MOFFETT CHARLES S.

N l A b nd hang f m

ma d m l med l re b

un C ur Egyp 1065

## MONONUCLEOSIS

f oc urt g urt ly w b

m l 1757

## MONTHLY MESSAGE

Am Med l A oc on 127 283

444 597 757 916 1067 1220 1381

1520 1668 1805

Berry F ank B f h

## MOORE JAMES E.

H gh C mo f Ryuky I l d

p p l p ak d d on f

Army h p l Okl wa 1224

## MOSELEY CHARLES H.

Surgeo U S Army J pan 1665

## MOSELEY HARRY G

ympo um on h zard

287

p f R ymoed F Long

A ard 590

## MOSQUITOES

on in tr l f 414

## MOUTH

l pom f l ca ry 1017

## MUDGETT CHARLES S.

m g f Army ul an and

b p l mmand 1222

p d L g f M in m t

m i 1518

## MUSCLES

pir ry GB po so d dog f

f f b w ur m sc l st m

l ( po den ) 600

## MYASTHENIA GRAVIS

d hym ma 1020

## MYCETOMA PEDIS

ad g ph hang 577

## MYELIN FORMS

unf d wh l b i f m

t f 507

## MYLERAN

m f hr n gran l cyt

l uk m 799

## MYOCARDITIS

mpl fl and influe

l k yndr m 488 491 493

b m d h um ar l

(CPC) 1639

## MYOCARDIUM

doc d l f b l st w h myo-

d l f ilur in i fan (CPC) 1319

## NATO

mul ry med al f f

A gus

## NAVY

A fl l l pe

w h 682 385 ( po d )

601

A fl mmun f

f y f 1720

Ce f f M t p d CIBA

Ph m l C p y 752

d l q men p d psy-

b urv y f 107

f g ff er nd ur

B h d 1519

K y Edw d C. pr mo d R

Adm l 589

l ur U S. N l School of

H p l Ad B h d

Md 1671

M l R lph W 1800

M half L f B w h f f

p bl d Bur f

Med d Surg ry N vy 1522

M d l nd D l Corp ff

l ct d for p mo d

m l 1377

M d l R h U N 3 Ca

Egyp h h ary 1802

l ac all d l

h p l 125

p h ar urg y xt oepor l

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e 1027  
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g f t g f 957  
p f w t b e l i s m g  
882  
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S u r g n G n e l d e s 282  
S c h t C r t i W c h f f d n t l  
d i 1800  
S l J h R w c m m n d o f  
a r c h t C o E g y p t 1065  
t r e p t c l p p h y l s i c r t  
543  
t b e l p d e m l g c s t d y f  
705 872  
t b r u l f l l w p t u d y f  
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c 1654

NEPHRECTOMY

f W l m t u m o s u r l f t r 561

NEPHROSCLEROSIS

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NEWS ITEMS

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r e t 1803  
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920  
A m e r a n D e n t l A s o c a n p r i n t  
m e t l S J d e n t a l  
d i a t p t o F E a 1066  
A n t w A r F c B h l  
d e l l O I  
A l g y P w s r 91  
A r m d F t e d a j m a m  
S u d a P e w M 41  
A r m p h a n y C l  
A r m y C o m C o m  
m a l 2  
A r m y m  
A r m y d e w r  
O m 1724  
A r m y m f

Berry Frank B p l e n h o n r r  
f e l l o w h i p i n I n t r n t i o n a l C o n f  
o f D e n t i s t s 129  
Berry Frank B p l e n M l a l o f f l n r  
i n P a r i s c e m n y 914  
Berry Fr k B h o o r a t u r k l l h r  
i A n k a r a 914  
B s k i A n t n y A r c e i v e s f i l l r o u p t  
A r d 1806

C t h o e B r i g G n e w A l i n t f r  
D e n t a l S i c U S A l 398

C e t l R p o i t o r y f o r M e l i c l  
C r d e n t i a l s W r l l M e l i c l A  
s t i 919

C r w f r d J o h n L p r o m o t e l 1007  
D C o u r s y l l b r t p r m o t l t o n a l r  
g e e l 1666

f r g n o f f c e r a t t e n l N a v y c u r a e  
1519

G r b y C p t r e c e i v e s H o f f M l l  
1224

h g h k i n g m d c a l o f f i c e r g l n  
h r a r y D o c t o r f S c i e c d e g r  
1064

H g A d m l g i e p r i t e n l i c e  
w t h P p P i s X I I 1218

H g a n A d m r l t N p l m e t  
P 915

J u r a l k c i l c t  
d 1068

K b k G A F r D t l  
C h f e c v L g o f M r t  
t u r m e 591

k y A m m e d t m t  
B U M E D h f 589

k m b g h S m h l d t W l t r  
R e d 126

K o b C L p d l f  
A m c C o l l g f P r t M d  
281

L a l d A F o c B H p t l  
d c d 131

M P l h W 1800  
f m A m y H o s p l d e d t e d t  
F r P T r a 1217

d e l a A l h m f  
A M A r t M l t r y M e d  
177

M h J f H d A m y  
f t r h d D e v l p m t  
f m m d l c f

m l d f m l m f  
122

l f f m t 002  
f f r h r e s c f l d

f f f 247  
f a e w c o l l n m e d  
g f f M e l c l



NEWS ITEMS (Co ed

MSTS p b w ho ary  
d gr f pur F D L y  
1671  
na IM d l d D I C rp  
f l ct d f pr m on  
d ural 1377  
N al Med al R ar h L N 3  
Caur Egypt b U S. Amb s-  
d U d A b R publ nd  
D N l D T r r f 1802  
N yl ctur U b N val  
Sch ol f H p l Adm tr io  
B he d Md. 1671  
N vy Med al D par me marks mile-  
to ucl armed 125  
N vy M d al R rv Co l  
B ardd g adua ra g  
pr g m 1219  
N vy C r t f l M t p d  
T F D H p d f  
CIBA Pharm al Company 752  
N vy Sc g N vy D k h d  
C l Aw d 760  
wh p l Ca II A F  
B ded d 1063  
wh p tal d d ed S tr A  
F B III 1670  
wh p l F R l y amed f  
G n. Ber d j h Dowl g l w  
h f gh g d ct 761  
N Ol k d Dan C.  
O l Sur G l f Air F  
1663  
Ogl D C. 1663  
po gr dua pr f so l ur  
ffer d M d 15 ff  
10 0 1672  
P d nr E h g l  
med l on ultant 123  
P d E h w mad h or ry  
f ll w f Amer Coll g f  
Surg 588  
R t P l l 1378  
P P 1 S et d 282  
Rus medic l l 1 b l  
592  
Seb Curt W d R j h  
Mal N vy d l h f 1800  
Se l j h R w mma f na l  
h un C Egypt 1065  
Se ood Army ul d h p l  
mma der me F r t Ge g  
M a. 1222  
S d C l b d phy alther p  
1276  
Sr p Col g Mur l f Omaha  
P Serv Aw d 28  
Th tr M d l Corps ff  
of Arm vy nd Aig F  
1 15

NEWS ITEMS (C ed

T pl Army H p l ry  
1522  
Tw h l l H ld H nam USAFE  
urg 124  
U S A F na nal ul  
and m m d urg me  
And w A F B 1517  
Vir h w c l l ur er  
no ed 1524  
W l R d h l  
p f m gl 450  
W ur k C p B nd  
Aw d. 449  
W g l nd Floyd L p m d  
br gad g oe l 1666  
Werg l d Floyd L uc d G  
R b E Dir f  
Dep nd Med P g m 1378  
W P Army H p l g  
cr d by J Co f  
A cr d f H p l 1223  
Wh B g C st l l d p den  
f Aer M d l A soc 590  
WHO F U S m g f ot f  
756  
W ld Co g f A M d ci  
1221  
W ld C gr f G oe l gy  
no f m g 448  
W ld H l h D y m a k s er ry f  
WHO 398  
Y Dr m d m d l e-  
h d 1226  
NIELSON CARL A.  
p f mer gl 450  
NIESS OLIVER A.  
uc ed D C Ogl Surg G  
er l f Air F 1663  
NITROGEN MUSTARD  
tr m f H dgk d d  
f l g y nd b 799  
NODULES  
hyr d 1558  
NOISE  
ANEHIN P j 1027  
BENOX udy b l g l ff  
f 1027  
CHABA mme ary 1027  
ff pe f m f p l  
1041  
h ar gl nd po ur high-  
ry 1038  
h b- ns ry ff l pe n-  
l 1027  
p y h ff f 1042  
NUCLEAR ENERGY Sec A m E gy  
NURSE CORPS  
Army po duat p f on l  
ur ff d 1072 1672

## NURSE CORPS (Co t n d)

Cl E th r ch f ur 8th  
Army 1665  
H y e I z Ch f f A y Nurs  
C r p i t Jap 1665  
H ght n R th A n m d D ctor f  
N y Nur C r p 753  
John o Ell ph t g ph tak t  
A my m d l fac lity F E t  
1665  
ff d th f See DEATHS  
S l i r D r thy sh f ur f m d  
l C t r J p 1665  
W r ck L B E g l  
P B d Aw d 449  
NURSES Se al Nurs C p  
A my C l W r p d 1310  
NUTRITION S l s D r Food  
ur y N r & F East 91  
Y m J h B m mb f N t l  
R earch C l C m m t t f r  
Qu t m t S b c m m t t  
N t t 1226

## OGLE DAN C

t ded c t on of ho p t l t Carsw ll  
Aur F B 1063  
t ded t o f ho p t l t L kl d  
A Fo c B 131 201  
c i D ing i h d Serv ce M d l  
1803  
retur 1663

## OKINAWA

m l a n 1758

## OLD AGE

C m m t t o Ag ng A M A 917

## OLIGURIA

ur b i t c d e dur g q em nt  
for red t i 370

## ORGANISMS Se und r pe if c m

E che b Sh g ll V b o

## OSLER WILLIAM

omm t o 1174  
D B i r r g mp f 662

## OSTEOMYELITIS

hr n s ur f t u d pain s  
mp t t tump 638  
rt b l nd th mb phleb t s n  
i f t 1336

## OTITIS MEDIA

h g l s s f ll w g d q  
t m t 1425

## OVALOCYTOSIS

d h m gl b C r t 1370

## PAGET S DISEASE

mo t t bo g f t r l m  
1508

## PAIN

bd m l s t h t  
l hyperl p m a 1418  
mp mp 635

## PAIN (Co tin d)

a d well ng of t r t r t r t r  
d i s 277  
c d c f tal over  
p ych ge ic m a s i f  
c r d c pecul t r s s  
fl ce f psy  
1184  
che r (CPC) 255  
ch t w th c uph  
1785  
l t ymptom of  
385 (c r r e pond  
ph t m l mb 644  
h ulde c sed  
m l ard ov sc l a f m  
lt g from M o r p

## PAKISTAN

tr tion s r e y in j l f

## PANCREAS

p mary myl d

## PANCREATITIS

t l hyperl p m a

## PARKINSONISM

Or nt l tr ted by c f r  
lid ct my 433

## PAROTITIS

p t p e t e 161

## PASTEUR LOUIS

Dr B ng m p r a s a f f

## PATHOLOGY

t 207  
p th l g t f l n s  
f t c c d t f t l t i  
pec m cho c qua  
p k g g of 843  
p me s h p m nt of 21

## PATTON JOHN F

dur t r f f i th f mbro  
S m na 126

## PENICILLIN

c r t r s t b l o d f c l e r  
p t t 370  
p phyl ct c p e g m f n t  
c l d 543

## PENTYLENETETRAZOL (Mott)

t dot t m prob m t 170

## PERGAMON INSTITUTE

R n med c l t l t s a  
f m 59

## PERICARDITIS

p c d g l l c g r  
p t m o c a l p m o l

## PERICARDIUM

y t d d t c l f 144

## PERITONITIS

f p p nd l g  
p p nd ct my wa t t m p  
h o p m l o d 1545

## PERPHENAZINE (T l f )

t l p t d t w th ph o m

## PERPHENAZINE (T i a l ) (C m d)

f w r y f l b l t y b l d r  
f l l w g f 745  
d f f t f 748

## PERSONNEL S l M d a l Off

P l R u  
k l l l l e d p y h i a  
u d y f 1745  
C l W l f r v d o c l  
w k p e 1298  
d l q m p d u r v y  
f 107  
d q u a l f f g a n f  
m e d f 1605  
J u r l k l i a o c  
e d o r 1068  
m l r y b m f 1436  
n a l f f f h g h y  
1027  
p y b l g d p u r  
h g h y n o 1040  
g m d l t a d a r d f  
f u l l m b l 1605  
p r y u d p b g  
d d f m p e n i 1286  
p b l y f f p  
f D u e  
t n d d a d f t r y  
J a r d (m e d l) 1613

## PERSONNEL ACTIONS

b g m e d l p l u a f  
21  
k l p e 33

## PHARYNX

b p h y g l d  
S p h y l (C P C) 1061

## PHILIPPINES

m l l p e u f p  
1753  
u r y 91

## PHLEBECTASIA

c a l m e d l m l d b y  
901

## PHYSICAL FITNESS

f A m e r y b 1067

## PICTORIAL FEATURES S N w l m

## PILLSBURY DONALD M

p p d f l l  
g r p 123

## PILONIDAL CYSTS

p m a r y p l k g f g f 957

## PLASMA S l s o a d a r b-

h d f B l o o d  
h m a p u r d p o o l d l l  
l f 1249

## PLASTIC

u g y S e S g r y

## PLEURA

l l p d m T u r k y l

## PLEURISY

b l w h f f p d m i c  
T u r k y l

## PLUENNEKE JOHN E

m m a d f L k i d A F  
B h p t a l 131

## PNEUMONIA

b h l S B a c h p m o 1785  
p l A f l 1574  
1576  
p l f l d  
f l l k y d r m 488 494  
p u m o c l p e a r d p d g  
l l g f 1359  
b m w h h u m  
f (C P C) 1639  
p h y l o c o c l (C P C) 1785

## POHL LOUIS K

w h p l C a w l l A F  
B u n d m m a d f 1063

## POISONING

u r h l d h g  
f f 1128  
G B p e d m l f B w  
u r m u s l u l f n  
d g p ( r r p d )  
600  
l d E D T A 989  
l g p h l p m d l g l  
844

## POLIOMYELITIS

n e u r l g l y m p m s p o b l y l d  
m f o r 1659

## POLLARD ERIC G F

m m d g f f f U S N l  
D l S h o o l 1800

## POPE PIUS XII

A d m l l l g g p u d  
w h P e P X I I 1218

## PORPHYRIA

b p w h p y h m  
f 1346

## PORTAL VEIN

h y p r t o n p a n p l p o  
g p h y 1257

## POTASSIUM CHLORIDE

d l o c d g m  
b m f 47

## POWELL WILLIAM H J

C h f M e d l O f f f S H A P E  
b q h o f F k B B r y  
914

## PRANTAL Se D p b m l M hyl

u l f

## PREDNISONE (M )

m e n f d m a m y 420

423

## PREGNANCY

d m y o c d w h 417

## PREPUCE

ga gr fll w gloc l n th i  
120

## PRESCOTT MANFRED U

t nf n f Ad is ry Counc l  
R er Aff is 751 (c r ton) 1065

## PRISONERS

of C nf d te d U arm 1594  
f war t b reul r t n 882  
urg o h ge f d r ng C il  
W 1595

## PROMOTIONS

na l M d l d D l Corps f  
f r l ct d for p m t t r e r  
dm r l 1377

## PROPYLTHIOURACIL

gr l cyt p n foll w g th py  
w th 571

## PROSTHESIS

cl ed d ct k t f mp t t  
st mp 639  
h d c m t gl for l t t r p t nt  
c t d f r 450  
mpt p r f t f mp t at  
st mp p 636

## PROTEUS

lg m ddl fect  
1433

## PSEUDOMONAS

r g n middle f t n  
1433

## PSYCHIATRY

m s luat f br g m d l  
pr ct 21

ch l d g d l c 1161

d l q t er em p d sur ey f  
107

gr p ther py th m d l p t t  
391

h gh t sty s eff ct of  
1042

hyp i A. M. A C n l

M t l H lth r port med l  
use of 1381

kl pt m 33

eur psych tr c d t nd

try t ton d rd n

m l tary s r c 1616

ph t m l mb p 644

p phy h p t w th p s hat c  
m f t 1346

s ck c ll r lled tudy f m l i s y

p r l t 1745

d t t mp th gh g t f  
or ub 728

c d t t mp th o d f

m prob m t 1692

t q l (m pr b mat) d l

t t mpt w th d 1692

ur ry n g r l d

## PSYCHIATRY (Cm r

t ur ter em f m n  
p bl m 121

## PSYCHOLOGY

c rd ac p f a m n

psych gen cm

hypn sis A M p

H alth r p res

me t l t t g r n s r g

Armed F c F n

te t dm sterat c

pos d t h gh

## PYELONEPHRITIS

hr (CPC)

## RABBITS

r bid subma illary g r n  
n 1772

## RABIES

tur lly eq red cara  
m xillary gl ad s f

## RADIATION

dose 318

and alkyl ting g r n  
fl cts f 797

b ol g l fl cts of 82

d lete ous eff t r n g r n  
1704

fl t s o blood n d h m r  
t 1705

e po u e cord of f  
Se w l t 862

hygien n ucles a m n

l g t m (l t) eff t r n f

m x m mp m i s i b l d s

maxim mp m i s s b l f

m d c l d o m m n s

m l tary p t of b i l r  
of 821

n l t m u r c e s of A  
f n l e a r b m b 647

n l a r s t i t y f m o i s a m

f l m t 648

of r m s w i t h c h l r

p ct o 1709

s i c k n d e s p t i n f r t

s u r c of 1704

synd m c m 3

RADIOACTIVE S l s

unde d d l h m i l

Rad och r m um

d cont m t w th h l a r e s

stanc s 990

f l l t f f c t

m d l r y f l m 648

fall ut f eld f o t p l

try elat h p b e w e n a r

k d n d m d l s

f l l t f m t h m

## RADIOACTIVE (Co ued)

ur lly wring l m k and  
l m y 1704  
d m p i d wit b m k o ub  
m 854

RADIOCHROMIUM (C<sub>51</sub>)

l b l g i d blood l l f d t  
m a g wh l l l m l uk m  
172

## RATS

m f food w b f  
p b bl mod f tran mus i f  
m l d 273  
an l i l f 414

## RAYDIN I S

d m g f Army ltan  
and b p l mmand 1222  
d m y m k g p i  
d E h w b ary f l l w f  
Am an Coll g f Surg 588

## REAGENTS S I T bai

L b m n-Bur b d Zak p dur  
f d m f um h l  
l 501

## RECORDS

m d l cr d l l po ry  
for l bl d ct 919

## RECRUITS

k ll t lled p y b  
udy f 1745

N vy p l p phyl i in 543

## REGISTRANTS

d q l f c f m d l  
1608  
m d l andard f f l l mobli i  
1605  
p g f by N l Sel  
S rv Sy m 1605

## K HABILITATION

m t glo W lt R d b  
let p f 450

## REILINGER ALFRED

In p G l f F h M l ary  
M d c l Se b q in ho  
f F k B B ry 914

## RESEARCH S I und pe f

b d g Rab l n l A an  
Army R ar h d D l pm t Com  
m d h d d by G M Nin b 1670  
p tm t w b urf e-ct b-  
an in f ma f my l form  
b t 507

in oa p b l gy 218

yp f f Ap l

Y m j b B pp d T h l

D f Re ar b for b Surg

G l f b Army 1226

## RESPIRATION

i d l g B w ur mus l i  
l f GB p d lm l  
( po d ) 600

## RESPIRATORY SYSTEM

A i flue 385 ( or po d )  
601

A fl F rt B l V

802

A nfl za w f l 264

1569

da f d y i  
dard m l ary rv 1630

lofl pid m d l ti f  
469

fl p d m h p i m

p n f Aur omy d APC 479

i fl pid m un ually

487

d p be ge d d

f mp

## RHEUMATIC FEVER

w h b m i p m i  
(CPC) 1639

l ard g ph fl f od m

l and po ium hl ld i 47

i m l ry p n n l 1436

## ROADMAN CHARLES H

d an d g d l l l w A

M d l A on 590

## ROBINSON PAUL I

E D f D p d

M d l C P g m 1378

## ROBINSON RUTH A

m d f urth h f f A my M d l

Sp li C p 1802

## RODENTS Se R and V

## ROENTGEN THERAPY

W lm um 561

## ROENTGENOGRAPHY

b l d g d by 1274

hang i myc m p d 577

d g i f g l h o

ph g l f l w b f

ph g 1015

f d g i A fl 1576

d g f p ard l y and

d rt l 1448

p lmo y d d g d by

1759

a y f med l y flm

l ar t d 648

un p d m d i l m f und

dur g i am 901

## ROSSITER PERCEVAL SHERER

f m S g G l U S N vy

d 282

## RYUKYU ISLANDS

secti d es t nc f hous fl  
68

## SANITATION

mp Co fed t Army 1581  
imp rt e in ecto t l 414  
U S S n tary Commis o C l W  
pe od 1300

## SARCROIDOSIS

l i l f t of 1759  
p lmo ary ro ntg g aph m fe t  
t s of 1760

## SATO KAZUO

P s d t f j p D t l As c  
atte d b nq t i ho of W l m R  
Alst dt 1066

## SAULNIER DOROTHY

b f aurs of m d c l c t n j pan  
1665

## SCHANTZ CURTISS W

l t d f p mot o t r ar dms l  
1377

d R lph M l s chi f f  
N y d st l d i n 1800

## SCHEIE HAROLD G

t f e c of Ad ry Coun lo  
R s rv Aff r 751 (corr t ) 1065

## SCHWARTZ JACK W

Tr pl r A my H sp t l und mmand  
f 1522

## SCHWICHTENBERG ALBERT

f rm Surg o f th Air D fe Com  
m d r t r 1378

## SCLERODERMA

w b ard d p lm ry f br  
(CPC) 399

## SCLEROSIS

m l pl my l fo m f und t  
l s s of 526 530

## SEAL JOHN R

b t t p b cc s f  
t th s y f f und g f n l  
M d c l R arch U t No 3 1802

## SEELEY SAM F

r t 1378

## SEMINAR Se M t g

## SERVICEMEN S l A For Army

M d c l Off N vy P nn l  
P lo R R g r a t  
d l q r p d sur y f 107  
phy l b t f d t b r  
l 722  
p n f w b al i mo g  
882

s rv b t of d t ber  
l 872

## SHELDON PAUL C.

C mb l ad Coun y M d l Soc e y  
m g 87

## SHIGELLA

dy t e i olat d in dysentery  
p d m c 965

## SICK CALL

co trol d p y hi tric study of m lary  
p rs l at 1745

## SIMMONS JAMES STEVENS

m m r l lectur 781

## SIMONS DAVID G

ad ced to grade of fell w Aero Me-  
cal Associ t o 590

## SKIN

d m t t he p t f rm t e ted w r s  
sulf py d 907

d m t my it n pr gn ncy 417

di se c ted w th d ab tes  
m l l i s 268

di s of and e try of retention  
tand ds in military s r ice 162,  
g lts t atment of large p loc t  
cy ts 957

c bi i l p d ca diab tic rsm  
m f st ti n f d ab t s mell t e  
1654

f mp r t d tump nd pain 637

s l od rma w th c rdi c d p l r f

f b osi (CPC) 399  
thomat of i senti l hyper-

p m a 1418

## SKINNER ROBERT B

r c key t Marti A my l l e r  
t d d tion t m y 1217

## SKULL

r p t f c an l defects foll lag  
f ctu s of 375

## SNAKES

c b om in f mation of 7  
f m i brai t s u 522

## SNOWDEN WILLIAM M

ad c d t g de f fellow A  
M d c l A s c s o 590

## SNYDER AGNES P

el ct d pre d t of Am l e a p /  
Th ry As it i n 1226

## SNYDER HOWARD McC

Wh t H phy c n i c r n  
m k g P sid t Els abow 110  
f l l w l Am an Coll g r f n  
588

## SNYDER OSCAR P

g b ry fellowship in k  
ti n l Coll g f Dent i

## SOCIAL WORK MEDICAL

f C l War p od 1290

## SODIUM LACTATE

d l c oc diagraphy in acu  
m f er 47

## SPACE FLIGHT

and s age  
pr ented m  
Surg ons

## SPACE FLIGHT (C ed)

hum l an m f h l  
 " p d 1093

## SPECIALTY BOARDS

An h l gy Am B ard f  
 288 594 919 1225  
 A M di Am B d f  
 P M di 133 1225 1379  
 1523  
 Ca d ul D Am an  
 B d f l ru l Med 1069  
 Cl l P h l gy Am B d f  
 P b l gy 1523 1807  
 D m l gy Am B d f 288  
 594 918  
 G col gy Am B d f  
 f ru l M d 918 1807  
 I l M d Am B d f 133  
 288 759 918 1069 1225 1379 1807  
 N ur l g l Surg ry Am an B d  
 f 288 919 1523  
 N ur l gy Am B d f Psy h  
 ry and N ur l gy 918 1807  
 Ob and Gyn l gy Am an  
 B d f 288 1069 1225 1379 1523  
 O p l Med Am an  
 B d f P M d i 1225  
 1380 1523  
 Oph halm l gy Am an B ard f 288  
 918 1069 1523  
 O l Surg ry Am an B ard f 1069  
 1225 1380 1807  
 O h p d Surg y Am B ard  
 f 594 759 918 1069 1807  
 Ot l ryug l gy Am B d f  
 288 918 1807  
 P h l gi An my Am B d f  
 P b l gy 1523 1807  
 P h l gy Am B d f 288 594  
 918 1379 1523 1807  
 P d tr Am B ard f 133 594  
 918 1379 1523  
 P d l gy Am an B ard f 133  
 919 1225  
 Phy l Med d R h b l  
 Am an B d f 1379 1523  
 Pl Surg ry Am B ard f 288  
 P M d Am an B ard  
 f 133 1225 1379 1523  
 P h d Am an B d f 133  
 594 1807  
 P y h ry Ame an Boa d f P y h  
 y d N ur l gy 594 918 1807  
 P y h ry d N ur l gy Am an  
 B d f 594 918  
 P bl H l h Ame B d f P e-  
 Med 133 1225 1379  
 Rad l gy Am Boa d f 133  
 594 1225 1379

## SPFCALITY BOARDS (C i d)

Surg y Am B d f 288 594  
 759 918 1069 1225 1379 1523 1807  
 Th Surg y B d f 288 919  
 1225  
 U l gy Am an B ard f 918 1069  
 1807  
 V i ary Publ H l h Am i  
 B d f 1225 1807

## SPHEROCYTOSIS

h d ary in 41 y l d m 1648

## SPINE

mp f ctur ( b l)  
 d by mm d p g i m b l  
 i 1736  
 b l my l i d hr mbo-  
 phl b i infan 1336

## SPLEEN

pr m ry y l d f (CPC) 1487  
 pl port g phy p an  
 po l hyp rt 1257

## SPLENOPORTOGRAPHY

p i port l hyp rt i  
 1257

## SPLINT

i d l f l pl i 39

## STAPHYLOCOCCUS Se M oc

STAPP JOHN P  
 g M l f Om h Publ Serv  
 Aw d 286

## STENOSIS

g l phag l (CPC) 77

## STINCHFIELD FRANK E

l ul Surg G l  
 f A F USAF 920

## STREPTOCOCCUS

f d h m f 1437  
 p ll p phyl ct p g m 543

## STREPTODORNASE

and p k i t m f ly  
 l d h m bor 949  
 and pod t m f ly  
 l d h m h 949

## STREPTOMYCIN SULFATE

on on i blood f l guri  
 p 370

## STRICKLAND BENJAMIN A. JR

l ct d m mb f E ut Coun l  
 A M d l A i i 590

## STRUGHOLD HUBERTUS

ad an d g d f f l l w A  
 M d l A i i 590  
 h m f pa fl gh  
 A M d l A me g 443  
 ip f Th doc C. Ly Awa d  
 f nd g h ev me in a-  
 p m d 590

## SUBMARINE MEDICINE

m di l d p rim d l N lus





## SPACE FLIGHT (C d)

hum l t m f h l  
t an p d 1093

## SPECIALTY BOARDS

An h l gy Am B ard f  
288 594 919 1225

A M d Am an B d f  
P M d 133 1225 1379  
1523

Ca d ul D Am an  
B d f l l Med 1069

Cl l f h l gy Am B d f  
P h l gy 1523 1807

D m l gy Am i B d f 288  
594 918

G l gy A B d f  
I m l M d 918 1807

I l M d Ame B d f 133  
288 759 918 1069 1225 1379 1807

N ur l g al Surg ry Am an B d  
f 288 919 1523

N ur l gy Am B d f P y h  
ry and N ur l gy 918 1807

Ob and Gy l gy Am an  
B d f 288 1069 1225 1379 1523

O p o l Med in Am an  
B d f P M d i 1225  
1380 1523

Oph h lm l gy Am an B d f 288  
918 1069 1523

O l Surg ry Am an B ard f 1069  
1225 1380 1807

O h p d Surg y Am c B ard  
f 594 759 918 1069 1807

O l yng l gy Am B d f  
288 918 1807

P h l g An my Am B d f  
P h l gy 1523 1807

P h l gy Am an B d f 288 594  
918 1379 1523 1807

P d Am an B ard f 133 594  
918 1379 1523

P d l gy Am an B ard f 133  
919 1225

Phy l Med d R h b l  
Am an B d f 1379 1523

Pl Surg y Am an B d f 288  
P M d Am an B ard

f 133 1225 1379 1523  
P b d Ame an B d f 133  
594 1807

P y h ry Ame an B d f P y h  
y d N ur l gy 594 918 1807

P y h ry d N ur l gy Am an  
B d f 594 918

P bl H l h Ame B d f P e-  
Med 133 1225 1379

R d l gy Am B d f 133  
594 1225 1379

## SPECIALTY BOARDS (C d)

Surg ry Am an B d f 288 594  
759 918 1069 1225 1379 1523 1807

Th Surg ry B d f 288 919  
1225

U l gy Am an B ard f 918 1069  
1807

V ur y Publ H l h Am  
B d f 1225 1807

## SPHEROCYTOSIS

h d ty in 41 y -old m 1648

## SPINE

mp f ur ( b l)  
d by mm d p s m b l  
1736

rt b f my l d hr mbo-  
phl b i i infan 1336

## SPLEEN

p m ry myl d f (CPC) 1487  
pl p rt s phy p an i  
po l hyp rt 1257

## SPLENOGRAPHY

p an port l hyp rt i  
1257

## SPLINT

d l f l pl 39

## STAPHYLOCOCCUS Se M

## STAPP JOHN P

s M ual f Om h Publ Se  
Aw d 286

## STENOSIS

s l ph s l (CPC) 77

## STINCHFIELD FRANK E

l l Surg G l  
f A F USAF 920

## STREPTOCOCCUS

f a d h m f 1437  
p fl p phyl p s m 543

## STREPTODORNASE

and p k in m f arly  
l d h m h 949

and p od rn i m f ly  
l d h m h 949

## STREPTOMYCIN SULFATE

on blood f l gur  
p 370

## STRICKLAND BENJAMIN A. JR

l ct d m mb f E ut Coun l  
A M d f A f 590

## STRUGHOLD HUBERTUS

d d s d f f l l w A  
M d l A 590

h ma f i pa f l gh  
A M d l A l me ing 443

pi f Th dor C. Ly Aw d  
f and s b ev me in  
p m d 590

## SUBMARINE MEDICINE

m di l d p rtm duri N ilus

## SUBMARINE MEDICINE (C t d)

d Se wolf 867

USS Na til s and USS Seaw lf  
851

rad ti p re 862

r diat o byg n a subma e 855

## SUBMAXILLARY GLAND

in tur lly c q i ed c i or l r b i s  
1768

## SUICIDE

attempt thro gh i g sti n f c r e  
bst nc 728tt mpt w tho erd fm prob  
m t 1692

## SULFAPYRIDINE

derm tit s h p t f mis 907

## SULFONAMIDES

i m ddle r infecti 1425

## SUNSTROKE Se H t St k

## SURGERY

mp t to t mppa 635

pp nd ctomy und b pt m l c d  
ti s 1545rdo l p d t c m n g m t  
f l t pr bl ms f ll w g 1155def it poste r olpor my f r  
p ur 157g aft ng p ma y pl t kin in tr t  
m t fl g pil d lcy t 957  
lia b grafts n r p of an s l  
d f cts 375limit d th tomy a d zymat c  
th appy i arly cl tt d hem th r  
949op h art t c rp l l t  
f r 1119pl tic l tie i milt ry h sp t ls  
1146

p st p r t e ar Bit h b y d

aft r b g l f t l n f r 20 m s  
f t p r t s of D c s

po t p r t e p ort 161

p l m n ry res ct s f tub culo s  
5 t 9 y f ll w p 363sur l f e r phre t my d part l  
phr ct my f b l t r l w l m s

t m rs 561

thym m wr g c l emo l f lti x  
i mi s f myasth gr s  
1026

l r c mpl t 359

l r p p r t i d op r t

of p tic t 355

## SWEAT

dph m l m thyl lf s t l f  
177

## SYMPOSIUM S M t x

## SYNDROME

W ll nb g r l x f m h mor  
h ge 1364

## SYPHILIS

Tr po m p l l d

F E t 9

TEACHING S T  
TECHNICScolp t my p s  
to 157F gl p r t t  
f d nt f  
498f d t cti f l  
f d t m e h  
172f d t f c t f h t  
f d t f c t f y  
846f d t f c t f l  
848f l t f v b  
f s m ch l t r o l dh m glob d t m t r p i  
t f e d dard 683e p r m t w th f  
t f m t f m y l t m  
f i d b t 507L e b m Bur h rd a t Z k  
p c d f det m t f m  
h l t r o l 501gan c b m d e b l g a l l d s  
p d d t f 498p t o f b i c t i o n f i l t  
pl c t d e t l p l t 39  
pl p o a p h y p r e t 1257pl t kin g r f u g p r m y i n t t  
m t f l g p l d l y t w 959i l g c d i g t c m i a  
ph l t s 1282Zak p c d i d t m i f  
s m ch l t e r l 501

## TELEVISION

col t d c t i l t r a w l e r  
R ed 180p r g m M U d e r t h S p r d  
by C I B A l h m t i l Comp y 752

## TERATOMA

f th y r o d g l d i l f 736

## TESTES

f l s f 740

## TESTS Se l T ch ic

Arm d Fo c Q l f at i 1606  
for d t i f h m a i i c i d i  
912for i l i f v b c m m 975  
h g h i n t y 1027ni a d t m t i f p  
f b r i d m l l y g l n d f  
b d d a 170p y b l a a t r l  
p o d e h g h n t i y 1040  
T r o m p l l d m m